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CHRONIC BRONCHITIS AND EMPHYSEMA

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Chronic bronchitis has been defined by Scadding as 'the condition of those patients suffering from chronic recurrent cough and expectoration, and usually effort dyspnoea, in whom these symptoms are not caused by disease of the lungs, by localized disease of the bronchi, trachea or upper respiratory tract, or by primary cardiovascular disease'. In Great Britain and other countries where climate and industrial air pollution together produce the ideal conditions for its development, chronic bronchitis and the later development of emphysema cause a heavy mortality and morbidity. In South Africa, fortunately, the disease is much less common, but still occurs often enough to make it an important illness to guard against by prophylactic measures, and to recognize and treat during the early stages of its development.

CLINICAL PICTURE

Most typically the condition begins with recurrent attacks of winter bronchitis, each attack being more persistent and more productive of cough and expectoration than the preceding bout. These attacks may start in early childhood and may then clear up for some years, or persist and progress year by year. The onset may, however, occur at almost any age; but there is always a heavier incidence in men than in women.

After a varying number of winters tightness and wheezing in the chest become noticeable, at first only during the bronchial attack, but later between attacks also. As the condition progresses this becomes a major feature of the disease, causing dyspnoea on effort and even at rest, sometimes with obvious attacks of 'bronchial asthma', while at the same time the cough tends to persist through the whole year with acute exacerbations during the time of the previous 'winter bronchitis' and also during any respiratory infection. Between these acute attacks the expectoration may be minimal and mainly mucoid, but with the superimposed infections the sputum increases in amount and becomes frankly mucopurulent.

Gradually the picture of emphysema develops, with the deep barrel-shaped chest, the hyperresonant note on percussion (obliterating the normal cardiac and liver dullness), noisy, wheezing and prolonged expiration associated with rhonchi over the lungs, and marked dyspnoea. In the preterminal stage polycythaemia and 'central' cyanosis develop and, almost inevitably, failure of the right heart follows, with increased jugular venous pressure, hepatomegaly and oedema of the feet. This is one type of heart disease to which the term 'cor pulmonale' is correctly applied, but in the past it has often been recorded on the death certificate as 'myocarditis', 'myocardial degeneration', etc. These cases show 'central' cyanosis, i.e., cyanosis of the tongue and mucous membranes in addition to blueness of the extremities, as opposed to the usual peripheral cyanosis of most cases of heart failure. The term 'black cardiac' has been coined for the most extreme cases of this type. Finally, the onset of drowsiness and confusion indicates that, unless treatment is effective, the end is near.

AETIOLOGY

(a) *Climate and Air Pollution*

As is to be expected, bronchitis occurs most frequently and severely where the winter is damp and cold, and in South Africa it is probably most seen at the Cape, although even here the winters cannot be judged severe as compared with countries such as England and Northern Europe. It must also be accepted that not only climate is important but also the heavy pollution of the atmosphere with industrial effluents and smoke and, where climatic and industrial conditions are combined, chronic bronchitis and emphysema have their highest incidence. During every fog, or more especially 'smog', there is always a sharp rise in hospital admissions for chronic bronchitis and respiratory illnesses, and also in the mortality from bronchitis and emphysema. Fortunately, heavy atmospheric pollution is also not common in South Africa, so that the combined effect of climate and industrial factors is seldom seen here. In highly industrialized countries such as England this association is common and both the incidence and the mortality of bronchitis are much higher in London and Manchester and in the industrial areas generally than in the countryside.

(*b*) *Smoking*

Various surveys of the effect of smoking have indicated that it bears a definite aetiological relationship to this disease. Even in the United Kingdom, where climate and air pollution are the major factors in the production of the illness, Doll and Bradford Hill found that in male doctors over the age of 35 heavy smoking caused a 6-fold increase in the mortality from bronchitis. The incidence of chronic bronchitis closely parallels that of carcinoma of the bronchus, which must be accepted as being associated with heavy cigarette smoking. Finally, duodenal ulceration, another disease of smokers, has a significant association with chronic bronchitis. That smoking produces bronchitis is not surprising; it is indeed so widely recognized by the laity, who have coined the term 'smoker's cough', that it is accepted as normal. One may presume that in the Union, where consumption of cigarettes per unit of population is exception-

ally heavy, and where the climatic and air-pollution factors in the production of chronic bronchitis are minimal, the aetiological significance of smoking is greatly increased. It is indeed unusual in this country to find chronic bronchitis and emphysema in non-asthmatic patients who are also non-smokers. It is surprising how little attention is paid to this factor both by patients and their medical advisers.

(c) *Constitution*

Constitutional factors undoubtedly are of very great importance in chronic bronchitis. These patients usually have a long history of cough, even dating back to childhood, or recurrent respiratory infections, nasal catarrh and repeated bouts of bronchitis can be traced, this tendency to 'weak chests' often being a familial one. Asthma and other respiratory allergies undoubtedly do tend to predispose to chronic bronchitis at a later period of life.

(d) *Infection*

The role of infection is also of considerable importance. These patients seem to develop respiratory infections very readily, and these infections are more persistent and severe than in other subjects. Exacerbations of established chronic bronchitis occur when respiratory infections are rife, but no particular organism can be incriminated, a variety of organisms being obtained from the sputum during exacerbations. Naturally enough, antibiotics have been employed for years in treating these acute infections, but more recently their use in prophylaxis has been under trial, with promising results.

PATHOLOGY

The nature of the essential lesions in chronic bronchitis is not clearly understood. Various authors have suggested that a primary disturbance of the mucus-secreting cells of the respiratory tract is the basic factor, the resulting swelling of the mucous membrane causing obstruction to the airway, especially in expiration. This expiratory obstruction, possibly in conjunction with a constitutional weakness of the alveolar walls of the lungs, causes breakdown of the alveolar partitions, which is the basic feature of emphysema. As a direct result, the pulmonary capillary bed is diminished and increased work is demanded from the right heart in the circulation of the blood through the lungs. The healthy myocardium of the right ventricle usually has no difficulty in maintaining a moderate increase in the pulmonary arterial pressure, and it is commonly only with the aging of the myocardium (around the age of 50-55) that embarrassment of the right ventricle becomes apparent. By this time alveolar destruction has reached an advanced state; at the same time ventilation of these damaged alveolar spaces is restricted by bronchial and bronchiolar obstruction, and impaired oxygenation of the arterial blood, with central cyanosis, results. Parallel with the reduction in oxygen tension in the alveoli, CO_2 retention occurs, so that the CO_2 tension in the arterial blood rises as the oxygen tension falls.

It must be emphasized that the cause of the arterial oxygen desaturation and the CO_2 retention is the impaired ventilation of the alveolar spaces, and that shunting of blood from the pulmonary artery to pulmonary vein by anastomoses is of little importance. Nor is a diffusion defect across the alveolar-capillary barrier demonstrable. With the deficient oxygenation of the blood, reflex pulmonary arteriolar contraction occurs, with a further rise in the pulmonary arterial pressure, further aggravated in many cases by secondary polycythaemia and increased viscosity of the blood, so that the stage is now set for failure of the overburdened right heart. Any respiratory infection, by causing further limitation of alveolar ventilation, may acutely precipitate the condition of central cyanosis, CO_2 retention and right heart failure, which, under favourable circumstances, may be as rapidly reversible if infection and spasm can be overcome. The chronic terminal condition, however, is more resistant to treatment, and chronic CO_2 retention ultimately causes the drowsiness, confusion and coma which, with failure of the right heart, is the main cause of death in these cases.

TREATMENT

Prophylaxis

(*a*) In patients who are subject to recurrent respiratory infections and winter bronchitis, the ultimate development of chronic bronchitis and emphysema is always to be feared, so that measures to prevent infection and irritation of the respiratory passages should be instituted at an early stage before irreversible damage has been done. As far as infection is concerned, avoidance of crowded, stuffy places, particularly during the season of respiratory infections, should be advised, but it usually is almost impossible to enforce this in patients who have to travel in buses to work, or who work in close proximity to others who may carry infections. Vaccines have been recommended and may be worth a trial, although convincing evidence of effectiveness is still lacking. Long-term prophylactic treatment with antibiotics, such as the tetracyclines in doses of 0·25 or 0·5 g. per day, has shown considerable promise. In carefully controlled experiments convincing evidence of a reduction in the frequency of attacks of bronchitis, and even an improvement in the condition of the lungs, have been obtained. Unfortunately, expense alone is likely to make this unacceptable to the majority of patients, and occasional toxic reactions also are a hazard. It seems likely that early treatment of acute bronchitis is a more acceptable method of prevention of further lung damage.

(*b*) Avoidance of bronchial irritation by smoke, dust or fumes is an obvious step, but may be difficult to implement in certain trades; consideration may then have to be given to the advisability of a change of work or residence, when this is possible. The obvious importance of a complete ban on smoking is unfortunately usually either overlooked or insufficiently stressed by the medical attendant, and nearly always meets with considerable resistance on the part of the patient. Frequently patients who have smoked heavily for years are ultimately forced to give up smoking when bronchitis with emphysema has already reached a crippling stage, but unfortunately it is then too late to expect more than slight relief of symptoms. It must be emphasized again that, especially in this country, smoking is one of the major causes of chronic bronchitis and emphysema.

(*c*) In the various geographical areas of South Africa there is a wide range of climatic conditions, so that sufferers,

or potential sufferers, from chronic bronchitis and emphysema can practically always find some part of the country where the climate factor can be eliminated; the cold and wet winters of the Western Province, particularly the Cape Peninsula, is obviously unsuited to these patients, and the climate of the Karroo or high veld, or possibly the Natal Coast, is much to be preferred. It is often difficult to persuade patients that such a major upheaval in their lives is justified or necessary, but where the condition is progressing year by year, there can be no doubt that such a change should be seriously considered.

Acute Bronchitis

Treatment of the acute attack of bronchitis follows the ordinary accepted measures, namely, rest in bed in a warm, well-ventilated room, antispasmodics (such as ephedrine, aminophylline or a combination of the two, and a sedative); and expectorant cough mixtures and inhalations. Expectorants have a time-honoured role but are of doubtful value, and inhalations of menthol, etc., also are mainly psychological in value; but a linctus containing codeine, heroin, opium, etc., is often necessary to ensure a reasonable night's rest from the distressing cough. Antibiotics are usually of the greatest value, especially when the sputum is mucopurulent in character, and preference should be given to the broad-spectrum antibiotics of the tetracycline group, or to novobiocin or chloramphenicol. Adequate dosage is essential during the severe phase of the cough, and at least 500 mg. 6-hourly should be given until a good response is obtained, when the dosage may be reduced to half this amount. Penicillin, or penicillin combined with streptomycin, is not usually as effective as the broad-spectrum antibiotics and, as the sufferer from chronic bronchitis is often also an allergic subject, the danger of penicillin reactions is very real. Steroids, such as cortisone, hydrocortisone, prednisone, etc., play little part in the treatment of bronchitis in the ordinary case, but where there is an allergic background they may be of definite value in speeding recovery. If a steroid is going to give relief, improvement is noticeable within 24-48 hours of its exhibition, and if this is not evident after 48 hours its use should be discontinued. Prednisone, 10-15 mg. 6-hourly, is a favoured preparation and, if effective, it can be maintained in slowly reducing doses for 10-14 days as necessary. Patients should be made to understand that any respiratory infection, even a minor cold, should be regarded as a major illness and should justify a period of treatment in bed, while the full routine outlined above should be instituted if any evidence of bronchitis develops.

Chronic Bronchitis

The more prolonged the chronic bronchitis, and the more severe the emphysematous changes in the lungs, the more severe the effects of each attack of acute bronchitis. Patients with advanced disease are usually willing to cooperate to the fullest extent in their treatment (except for the question of giving up smoking) but it is impossible to reverse the structural damage to the lungs, so that the results of treatment cannot be really satisfactory; obviously it is of great importance to insist on adequate prophylactic measures in younger patients before the full-blown picture of chronic bronchitis and emphysema develops.

Cor Pulmonale

In patients who are already cyanosed, an acute bronchial attack is a major illness which may terminate fatally, and treatment is a matter of urgent importance. Cardiac failure may develop, producing a rise in jugular venous pressure, hepatomegaly, and oedema of the legs. Increased cyanosis, so that the tongue becomes a dark blue colour, is then to be expected, while consciousness becomes dulled and the patient drowsy and stuporose. The development of coma is usually a pre-terminal event. Treatment here is the same as for any acute attack of bronchitis, and a response to antibiotics offers the best hope of recovery. In addition, mersalyl, 2 c.c. every 2nd or 3rd day, may be of great value, or chlorothiazide, 2-4 tablets (1 to 2 g.) daily, may be substituted. Diamox may be especially useful, because it has some effect in lowering the CO_2 tension of the blood in producing its diuretic effect. It certainly is worth a trial in severely ill patients. Full digitalization is recommended, but may have disappointingly little effect on the degree of heart failure. The administration of oxygen is obviously suggested by the cyanosis, but it should be used with caution because it may cause deepening of the stupor and even coma and death. In these patients the prolonged and excessive degree of CO_2 retention leads to a blunting of its normal stimulating effect on the respiratory centre, and lowered oxygen tension of the arterial blood is the main respiratory stimulus; if this is removed by free administration of oxygen (as in an oxygen tent), the respiratory efforts are diminished and the patient rapidly becomes more comatosed owing to a rise in the arterial CO_2 tension although, paradoxically his colour improves and cyanosis may be absent. Oxygen therefore should be given only by nasal catheter, preferably intermittently, and at the first sign of increased unconsciousness it should be stopped until consciousness is again restored. Where facilities are available for assisted respiration, oxygen may naturally be given freely with much benefit to the patient. Ideally, in the comatosed case a tracheotomy should be performed, and IPPR (intermittent positive pressure respiration) can then be applied with considerable benefit, and at the same time secretions can be aspirated from the trachea and bronchi. Aminophylline, 0·25 or 0·5 g., should be given by intravenous injection, and 'solucortef' should be given at the same time (100 mg. intravenously). It has recently been suggested that large doses of amiphenazole, e.g. 150 mg. intravenously per hour, may be useful because of a specific stimulating effect on the brain and respiratory centre, and in promoting cough and expectoration. It is clear, however, that the prognosis is poor, and that treatment should be undertaken only in a hospital where full facilities are available. Even then, in spite of the best possible treatment, failure to respond is common enough, while improvement can of necessity only be temporary.

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EDITORIAL : VAN DIE REDAKSIE

PORPHYRIA IN SOUTH AFRICA

Until a few years ago porphyria was considered to be a very rare disease, although it had been reported from many parts of the world. Congenital or erythropoietic porphyria,[1] which causes pink staining of the teeth and bones and marked light sensitivity from birth, is inherited as a Mendelian recessive trait. Only 36 authenticated cases have been reported in the world literature.[2,3] In cattle it is known as pink-tooth disease.

Waldenstrom, of the University of Lund, who carried out pioneer work on porphyria, described a type of porphyria that is common in the North and comparatively rare in the South of Sweden. His suggestion that the general incidence of porphyria in Sweden is 1·5 per 100,000 inhabitants, is perhaps an underestimate.[4] This type of acute intermittent porphyria is inherited as a non sex-linked Mendelian dominant trait. There is no increased skin sensitivity to sunlight or injury, but an acute attack of porphyria may be precipitated by the use of certain drugs, particularly barbiturates and sulphonamides. The acute attack is characterized by abdominal and muscle pain and by marked emotional disturbance; it may proceed to generalized peripheral neuritis, and perhaps the death of the patient. During the quiescent phase there is, in this type of porphyria in adults, a great excess of porphobilinogen and delta-aminolaevulic acid, precursors of porphyrin in the urine, and the Watson-Schwartz test with Ehrlich's aldehyde is positive. There is little or no increase in the faecal porphyrin.

Porphyria is very common in the White population of South Africa, among whom it is also inherited as a Mendelian dominant trait.[5-7] It also occurs among the Coloured people. Porphyria, which is relatively common in South Africa, was introduced by an early settler from Holland, whose descendants have multiplied extremely rapidly under ideal conditions. Today, one million of the three million White people in this country bear the names of 40 original settlers, and it is interesting to contemplate that all the male members of these families, illegitimacy apart, inherit their Y chromosome from 40 original free burghers. Dean[8] claims that he has traced 38 large groups of porphyric families to one original ancestor, Gerrit, the son of Jan, who married at the Cape in 1688, and he considers that they have inherited porphyria from Gerrit or his wife Ariaantje.

The Mendelian dominant type of porphyria, which is common in South Africans, is a different genetic disorder from the acute intermittent porphyria described by Waldenstrom.[9] The South African type, porphyria variegata, is characterized by acute attacks precipitated by drugs, and often by light sensitivity of the exposed skin. South African porphyria may be symptomless except for a high excretion of porphyrin in the faeces and some increase in urinary porphyrin. Acute attacks occur more frequently in women, and the skin sensitivity is usually more marked in men. When there are no sores or scars on the back of the hands, the skin may still abrade easily if scratched with the finger nail—a useful clinical test. In the acute attacks the urine is often port wine in colour, and the Watson-Schwartz test for porphobilinogen is always positive. In the quiescent phase the urine is normal in colour, the Watson-Schwartz test is negative, and there may be only a slight increase in urinary porphyrin. However, in both the acute and the quiescent phases there is a great excess of porphyrin in the faeces, unlike that in acute intermittent porphyria.

The easiest way to screen the faeces for excess porphyrin is to prepare a solution of a small fragment in 2 ml. of a solvent consisting of equal parts of glacial acetic acid, amyl alcohol, and ether. When this brown solution is examined in ultraviolet light with a Wood's filter, its colour is normally green or grey. A brilliant pink fluorescence suggests the possibility of porphyria, and the patient and the family should be investigated clinically, and a quantitative analysis of the porphyrin excretion in the urine and faeces should be undertaken. A great excess of chlorophyll sometimes gives a pink fluorescence. Excess of porphyrin in one specimen of stool does not necessarily mean that the patient is a porphyric; further investigation will confirm or refute the diagnosis.

During the past six months an interesting pilot experiment in routine testing for porphyria has been carried out in Port Elizabeth. All patients admitted to hospital in Port Elizabeth have been subjected to a routine test for porphyria before the administration of pentothal, other barbiturates, or sulphonamides. An account of this experiment will be given at the South African Medical Congress in East London towards the end of this month.

Barnes[10] describes a disturbance of porphyrin metabolism with light sensitivity which is common among the Bantu. There is no evidence that this is a hereditary disorder; it would appear to be due to a disturbance of liver function, often secondary to malnutrition and the use or abuse of adulterated alcoholic beverages. This type of porphyrin disorder is accompanied by a high excretion of porphyrin in the urine, but little or no increase in the faeces. It would fit into the group described as porphyria cutanea tarda symptomatica. As Garrod[11] defined porphyria as an 'inborn error of porphyrin metabolism', it is a question of semantics whether a disorder of porphyrin metabolism that is not inborn should be called porphyria. In this type of por-

phyrin disorder skin lesions may be severe, but attacks of acute porphyria do not occur.

Acute porphyria is an extremely serious illness and a threat to the patient's life. The correct diagnosis is often missed and, when it is made, treatment necessitates a very high level of medical and nursing attention and is not always successful. Prevention of the acute attack will save much suffering. Prevention depends on considering the possibility of porphyria and excluding it before prescribing barbiturates and sulphonamides. In Dean's view, patients in South Africa should be screened for porphyria as a routine, especially before the administration of a pentothal anaesthetic. When porphyria is diagnosed, all the relatives who can be traced should also be screened for the disorder. Porphyrics should be warned of the extreme danger of taking certain drugs, and should be given a letter describing the evidence for the diagnosis. This letter should be shown by the patient to any doctor whom he or she may consult.

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DIE VERENIGING VIR GEESTESGESONDHEID

Gedurende die afgelope aantal weke het die *Tydskrif* eksemplare ontvang van die jaarverslae van al die verskillende takke van die Vereniging vir Geestesgesondheid. Die groot en belangrike werk wat hierdie Vereniging dwarsdeur die land doen word duidelik in hierdie verslae weerspieël, en almal wat in die werksaamhede van die Vereniging belangstel word aangeraai om met die oog op verdere besonderhede in verbinding te tree met die Sekretaris van die Suid-Afrikaanse Nasionale Raad vir Geestesgesondheid.*

Die Vereniging vir Geestesgesondheid bestaan al sedert 1918 en is soos volg saamgestel: In die eerste plaas is daar die algemene koördinerende en beleidvormende liggaam: die Suid-Afrikaanse Nasionale Raad vir Geestesgesondheid. Verder bestaan die Vereniging uit 10 takke of susterverenigings wat versprei is in die groot dorpe en stede van ons land.

Ons het al by verskillende vorige geleenthede[1-3] gewys op die onbevredigende toestande wat hier geld ten opsigte van die versorging en behandeling van geestesongesteldes. Omdat ons in Suid-Afrika nie beskik oor genoegsame doeltreffende kliniese dienste op die gebied van die psigiatrie nie, is die dienste wat die Vereniging vir Geestesgesondheid lewer van des te groter belang.

Die volgende is 'n baie beknopte beeld van wat hierdie Vereniging doen op al die plekke waar hy takke het: Die Vereniging reël en organiseer gereelde klinieke op 'n buitepasiënte-basis vir persone wat aan enige vorm van ligte of ernstige geestesversteuring ly. Ook reël hy klinieke vir verstandelik vertraagde en swaksinnige kinders en persone, en kinderleidingklinieke. Deur middel van spanne maatskaplike werksters word gevallewerk en gesinsorg op groot skaal onderneem. Die mediese professionele werk in die klinieke word waargeneem deur mediese beamptes van die Departement Gesondheid—beamptes wat psigiatriese werk doen in die verskillende hospitale vir geestesongesteldes.

Die bronne waaruit hierdie Vereniging put om sy administratiewe en finansiële verpligtinge na te kom, is soos volg: Elke tak van die Vereniging ontvang 'n jaarlikse subsidie van die Nasionale Raad, wat op sy beurt weer gelde ontvang uit openbare bronne sowel as 'n aansienlike toelaag van die Departement Uniegesondheid. Gedurende die afgelope jaar was daar sprake dat die Departement Gesondheid besig is om die verdere toesegging van dié toelaag in heroorweging te neem. Ons wil hier graag die geleentheid gebruik om die Departement—wat die Vereniging in elke geval baie goedgesind is—dringend te versoek om, indien enigsins moontlik, daardie toelaag nie terug te trek nie, maar eerder te vergroot. Dit sou 'n ernstige slag beteken vir verskeie takke van die Vereniging as hulle nie meer kan reken op daardie bydrae nie.

Elke tak van die Vereniging ontvang ook ondersteuning uit verskillende openbare bronne uit die gebiede waar hulle werksaam is. In die belang van die toekoms van die dienste wat op hierdie gebied gelewer word, is dit egter uiters noodsaaklik dat die samestellende dele van die Vereniging probeer om finansieel so onafhanklik moontlik te word.

Ons leef in 'n tyd waarin daar 'n groeiende bewustheid is van die groot rol wat geestesgesondheid, en die beginsels waarop dit berus, speel in die nastrewe van beter aanpassing en 'n gesonder en gelukkiger wêreld in die algemeen. Hierdie groeiende bewustheid van die betekenis van geestesgesondheid is nie net waar te neem in ons eie land nie, maar dwarsoor die hele beskaafde wêreld. Die Wêreld Federasie vir Geestesgesondheid, waarvan die Suid-Afrikaanse Nasionale Raad vir Geestesgesondheid 'n stigterslid is, het juis die jaar 1960 as Wêreldgeestesgesondheidsjaar aangedui. Die doel met hierdie voorgenome plan is om nuwe belangstelling te wek vir die werksaamhede van die internasionale en nasionale organisasies wat dit vir hulself ten doel gestel het om 'n groter mate van geestesgesondheid vir soveel mense as moontlik na te streef. Om hierdie rede is dit dus ook van pas dat ons nou al navraag doen na waar ons ten opsigte van hierdie verpligting staan—wat betref alle moontlike dienste soos wat gelewer word deur die Vereniging vir Geestesgesondheid, die Unie- en Provinsiale Gesondheidsdepartemente, plaaslike hospitale, private psigiaters en geneeshere, en die algemene publiek.

1. Van die **Redaksie** (1958): S. Afr. T. Geneesk., **32**, 652.
2. *Idem* (1958): *Ibid.*, **32**, 996.
3. *Idem* (1959): *Ibid.*, **33**, 269.

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EXPERIENCE WITH PERICARDITIS AT GROOTE SCHUUR HOSPITAL, CAPE TOWN

AN ANALYSIS OF ONE HUNDRED AND SIXTY CASES STUDIED OVER A SIX-YEAR PERIOD

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In Cape Town we have a multiracial society living under the same climatic and geographic conditions, with each race, in the main, adhering to its own traditional customs, particularly as regards diet. The Whites, are mostly derived from Great Britain, Holland and France. They are economically privileged; even the patients who attend the public hospital (Groote Schuur), although representing the poorer section of the White community, earn considerably more than the average non-White. The Cape Coloured community originated mainly from White, Hottentot and 'Malay' stock; only within the last few decades has any Bantu element been added. The Hottentots were the original indigenous population of the Cape. From the socio-economic point of view the Cape Coloured occupy a position midway between that of the White and the Bantu. Like the White, they are a relatively stable population and, for the most part, have lived all their lives in an urbanized community and have been exposed to all the infections and diseases that are common to city dwellers.

The Bantu, descendants of migrant tribes from Central Africa, occupy the lowest place in the socio-economic scale, providing the unskilled and heavy labour. They are an unstable population migrating from the rural parts of South Africa for a temporary stay of one or two years. During this period they attempt to meet their own needs and the needs of their homes in the Reserves.[1] As a consequence there is a strain on their meagre resources which contributes to the development of malnutrition and the consequent lowering of their resistance to infectious disease. Moreover, as they live in overcrowded and often insanitary conditions, it is not surprising that the incidence of infectious disease in this racial group is high.

When it is remembered that the Western Province, of which Cape Town is the capital city, is the chief wine-producing centre of one of the great wine-producing countries of the world, it can readily be appreciated that the effects of alcoholism are often superimposed on those of poverty, overcrowding and malnutrition. One would therefore expect that the diseases associated with the underprivileged, namely deficiency disease and tuberculosis, would occur frequently in the Coloured and Bantu racial groups.

As far as the cardiovascular system is concerned, this results in a great incidence of pericarditis, which is usually tuberculous in origin, of beri-beri heart disease,[2] and probably of 'cardiac failure of unknown origin'.[3]

During the 5 years July 1952 to June 1957, 160 consecutive cases of pericarditis have been reviewed in the Cardiac Clinic, Groote Schuur Hospital, and their course has been followed until August 1958. Pericarditis complicating rheumatic fever, the collagenoses, uraemia and cardiac infarction have been excluded from this study. It is usually not difficult to differentiate pericarditis from 'cardiac failure of unknown origin' and beri-beri, though on occasions special techniques such as cardiac catheterization or even exploratory thoracotomy may be necessary.

This study is concerned with the aetiology, natural history and results of treatment, including surgery, in these 160 cases of pericarditis.

MATERIAL AND METHODS

During the 5-year period under survey the electrocardiographic (ECG) service of the Cardiac Clinic included all in-patients and out-patients attending Groote Schuur Hospital and the 44 in-patient beds of the Somerset Hospital. As previously described,[3-5] all patients suspected of having heart disease have ECGs performed and all tracings have been examined by the author. During the period under review, approximately 22,000 ECGs were studied. Where the diagnosis of pericarditis was suspected on clinical or ECG grounds, the case was selected for special study. In this way 160 consecutive cases of pericarditis were obtained, representing all the cases of pericarditis recognized as such occurring in these two hospitals during the 5-year period under review.

Of the 160 patients, 69 were under the personal care of the author, and 67 were seen in consultation and followed through their illness while in hospital. Of the remainder, 11 were first examined after discharge from hospital, 8 died before they could be examined, and only 5 were never seen and were untraceable.

All patients were advised after discharge to attend the special pericarditis follow-up in the Cardiac Clinic for long-term treatment, usually anti-tuberculous, and observation. Whereas local White and Coloured patients are relatively easily controlled in this way, the Bantu present a far more difficult problem. As their stay in the city is often temporary, they cannot be re-examined over a period of many years. They are frequently untraceable from their local addresses and the importance of prolonged treatment is not usually appreciated. However, with the assistance of a trained

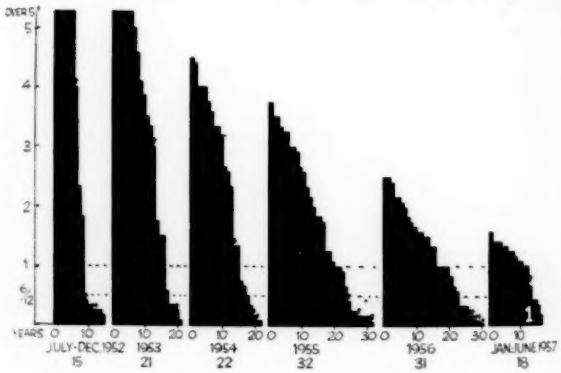

Fig. 1. Follow-up period. 75% of the patients were seen for periods longer than 6 months. Many of the patients seen for less than 6 months (10%) had died of their disease (†). These figures include the 139 cases of tuberculous, probable tuberculous and pericarditis of unknown cause only.

social worker, it was possible to follow up the majority, though reliance on general practitioners' reports were sometimes necessary. Once repatriated to the Territories, follow-up by correspondence was the only possible means, and was usually unsuccessful. During the first year of follow-up, patients were seen frequently but thereafter, except for surgical cases, who were seen more frequently, they were examined at yearly intervals.

The majority of patients were adequately studied, follow-up study including clinical, ECG and radiological examination. In this way 92% (147) of all patients were personally seen at some time in their illness, and follow-up was possible and adequate in 94%.

The material was divided into two groups. In the first were included tuberculous and probable tuberculous pericarditis and pericarditis of unknown cause, and in the second, pyogenic and a few miscellaneous causes. The follow-up period in the first group is shown in Fig. 1. The majority of patients (75%) were seen for periods longer than 6 months, by which time the condition is usually cured or static. Many of the patients seen for less than 6 months (10%) had not survived this period and had died of their disease. In the second group, the mortality rate was higher but the majority of the survivors were followed up for an adequate period up to 3 years.

The sex, race and age in the 160 cases of pericarditis is analysed in Table I. The maximal incidence was between the ages of 20 and 50 (60%), except in the pyogenic group, where the condition occurred earlier. Males were affected more than 3 times as commonly as females, especially in the tuberculous series. Pericarditis was uncommon in Whites, who made up only 8% of the cases, though the attendance of Whites at the hospital is equal to that of the Coloured.[2] On the other hand, over 50% of the cases of pericarditis occur in the Bantu, though this race represents, only 1/5th of the hospital population.[6] In fact pericarditis is one of the commonest cardiovascular diseases in the Bantu.[3] Pericarditis is far commoner in the Coloured than in the White, but less common than in the Bantu.

In addition to the aetiological diagnosis the cases were analysed according to whether pericardial effusion or constrictive pericarditis was present. (*a*) The diagnosis of pericardial effusion was based on the finding of a pericardial friction rub, aspiration of the pericardial fluid, and clinical and radiological evidence of considerable enlargement of the cardiac outline. On treatment, significant reduction in the heart size occurred. Cardiac compression was often present (tamponade), reflected in jugular venous distension, hepatomegaly or oedema on the right side and pulmonary congestion with dyspnoea on the left. Pleural effusion was common, but it was often inflammatory and not mechanical. On the other hand, tamponade was not invariable; many cases even with big effusions showed no signs of interference with cardiac function. (*b*) In the constrictive pericarditis group, either following absorption of the pericardial fluid or presenting *de novo*, marked evidence of cardiac constriction was present. Pericardial friction rub was absent, pericardial aspiration failed to yield fluid, and the heart size was normal or only moderately increased. Jugular venous distension and hepatomegaly were always present, and oedema, pulsus paradoxus and pulmonary congestion were often found. Treatment of the cardiac failure produced partial relief only. Surgery was performed in 45 cases of constrictive pericarditis and in only one was there still some fluid present, though marked constriction dominated the findings.

DIAGNOSIS

The diagnosis could usually be made by the clinical methods in common use, including ECG and radiology. A history of pain of pericardial origin occurred in about 60% (94) of the cases and was the most valuable single finding extracted from the history. Though occasionally mistaken initially for the pain of ischaemic heart disease, the differentiation was usually relatively easy, because of the stabbing quality of the pain, the relation to respiration and the associated ECG and radiological findings. Pericarditis was often associated with pleurisy (20%) and this frequently gave rise to both pericardial and pleuritic pain occurring simultaneously, unlike that which occurs in ischaemic heart disease. In the Bantu, a history of pain in the centre of the chest almost always indicates pericarditis, as ischaemic heart disease is so exceptional.[7] In the White and Coloured, however, in whom coronary disease occurs so frequently, the differentiation of ischaemic pain from the pain of pericarditis must be made. Difficulty arose chiefly in cases that were considered to have 'benign pericarditis', as in this condition the onset was often so sudden and the duration of pain relatively short. Other symptoms of cardiac involvement, such as effort dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, hepatic pain and systemic congestion, were frequent but were of no assistance in anatomical diagnosis.

At some time in the illness, a pericardial friction rub was heard in 50% of the cases (81) (Fig. 2) and in 40% the friction rub was present on the initial clinical examination.

TABLE I. SEX, RACE, AGE AND AETIOLOGY IN 160 CASES OF PERICARDITIS

Age	*Tuberculous*					*Presumed Tuberculous*					*Unknown*					*Total*	*Pyogenic*					*Miscellaneous*					*Total*
	M	*F*	*W*	*C*	*B*	*M*	*F*	*W*	*C*	*B*	*M*	*F*	*W*	*C*	*B*		*M*	*F*	*W*	*C*	*B*	*M*	*F*	*W*	*C*	*B*	
0—9	5	2	0	5	2	0	0	0	0	0	1	0	1	0	0	9	4	1	1	4	0	0	0	0	0	0	14
10—19	11	5	1	14	1	2	3	0	2	3	0	2	1	1	0	22	1	2	0	3	0	0	1	0	1	0	26
20—29	10	2	0	5	7	5	2	1	0	6	6	1	2	3	2	27	2	3	0	5	0	0	0	0	0	0	32
30—39	11	2	1	2	10	12	2	0	4	10	4	1	0	1	4	31	1	0	0	1	0	0	1	0	0	1	33
40—49	15	0	0	3	12	10	0	1	0	9	4	1	0	1	4	30	1	0	0	1	0	0	0	0	0	0	31
50—59	6	0	0	2	4	4	1	1	1	3	1	0	1	0	0	12	2	0	0	2	0	1	0	1	0	0	15
60	2	2	0	3	1	3	0	0	1	2	1	0	0	0	1	8	0	0	0	0	0	0	1	0	1	0	9
Total	60	13	2	34	37	36	8	3	8	33	17	5	5	6	11	139	11	6	1	16	0	1	3	1	2	1	160

Males (M) 125. Females (F) 35. White (W) 12. Coloured (C) 66. Bantu (B) 82.

Pericardial aspiration was successful in 44% (70 cases), the fluid usually being blood-stained and, with one exception, inflammatory in nature. A pericardial friction rub or pericardial aspiration thus proved the diagnosis of pericarditis in 66% of the cases (107). Surgery was performed in 47 cases,

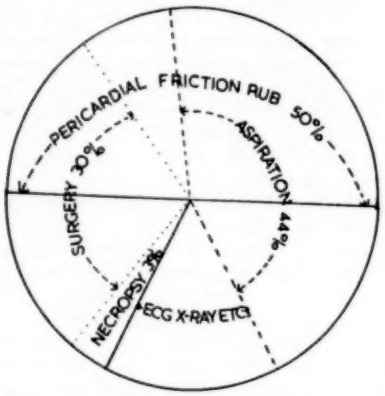

Fig. 2. Diagnosis of pericarditis, 160 cases (see text).

in 23 of whom no friction rub or pericardial fluid had been found. There were 5 cases in whom the clinical diagnosis was confirmed by necropsy only. Thus in 84% of the 160 cases (135) the diagnosis was proved by the presence of a pericardial friction rub, aspiration of pericardial fluid, surgery or necropsy. In the remainder, the diagnosis was based on clinical, ECG and radiological findings (Fig. 2).

The majority of cases could be diagnosed at the bedside. Other investigations included phonocardiography, kymography, venous pressure and circulation times, cardiac catheterization and selective angiocardiography, but these refined methods of investigation were of value in an occasional case only. There remained a few cases in which it was not possible to differentiate pericarditis from 'myocardial failure of unknown origin' with absolute certainty. Two patients early in the series were in fact subjected to thoracotomy to exclude the diagnosis of constrictive pericarditis. The number of cases where the diagnosis was uncertain, however, was extremely small and they were excluded from this series, since they would have no bearing on the statistical value of this study. Common cardiac diseases such as hypertension, coronary vascular disease and valvular disease were readily excluded and did not give rise to difficulty in diagnosis.

AETIOLOGICAL DIAGNOSIS

After excluding rheumatic heart disease, collagenosis, uraemia and cardiac infarction, the common causes of pericarditis in this series were tuberculosis, unknown infections (presumably virus), and pyogenic organisms.

1. *Tuberculous Pericarditis*

Acid- and alcohol-fast bacilli morphologically identical with *M. tuberculosis* were isolated by culture or guinea-pig inoculation from 27% (13) of the 49 cases in whom the pericardial aspirate was examined for these organisms. Many of the fluids in which organisms were not isolated were nevertheless tuberculous. This was proved by the finding of a tuberculous histology at surgery performed at a later stage in 9 cases in whom the bacteriology of the fluid had been negative. There were 2 additional cases in whom pleural-fluid examination was positive for tuberculosis and 1 in whom the ascitic fluid was positive, so that it was fair to regard the associated pericarditis as tuberculous in nature. A positive histology was obtained at surgery in 25 further cases and at necropsy in 3. Absolute proof of tuberculous pericarditis was, therefore, obtained in 44 cases.

In 29 cases there was overwhelming clinical evidence that the pericardial infection was tuberculous, in view of active tuberculosis elsewhere. Active pulmonary tuberculosis was present in 7, in 4 of whom a positive sputum was obtained. Involvement of hilar and peripheral glands by tuberculosis was present in 11 and, in addition to the adenopathy, there was sometimes evidence of involvement of other organs such as the pleural cavity, eyes and spleen. In some cases long-term follow-up revealed the development of glandular calcification radiologically. In 3 cases, miliary tuberculosis was shown by liver biopsy and, in addition, adenopathy and hepatosplenomegaly were present. There were 3 cases with peritonitis, the features of which were those associated with tuberculosis, and glandular enlargement was also present in one of these cases. Meningitis with the features of tuberculosis was present in 2 and osteitis in another 2. One afebrile patient had a loculated pericardial effusion from which sterile pus was withdrawn, as well as deeply haemorrhagic fluid from another loculus. Pleurisy developed later. Constitutional symptoms, pyrexia and response to antituberculous therapy in almost all these cases were additional features suggesting a tuberculous origin of the pericarditis. There were thus 73 cases of pericarditis which were almost certainly tuberculous in origin.

There were only 2 tuberculous cases in Whites (Table I), whereas 34 were in Coloured and 37 in Bantu. Over half the Coloured cases occurred in patients under 20, whereas the peak age in the Bantu was between 30 and 49. This is presumably due to the fact that the Coloured are a stable urbanized population with a high incidence of tuberculosis of all forms and a high infectivity rate, hence the infection of children at a young age. The Bantu are a migrant population with relatively few permantly urbanized families born in Cape Town and the high incidence of the disease between the ages of 20 and 49 is presumably related to the fact that the majority of the 'population at risk' fall between these age groups.[4] In the 37 Bantu patients there were only 2 females; this is in part related to the male predominance in the Bantu population previously mentioned.[6]

2. *Probable Tuberculous Pericarditis*

There were 11 cases who presented for the first time with well developed constrictive pericarditis; in 9 of them operation was followed by the histological finding of fibrous or granulation tissue without tubercle follicles. It is reasonable to assume that the majority of these cases were, in fact, tuberculous in origin, though constrictive pericarditis has been attributed to other causes.[5, 9] Most of the cases were chronic, of long standing, and some even had extensive calcification, so that a negative histology was not unexpected. Moreover, it must be remembered that the intensive and often prolonged antituberculous therapy which preceded histological examination at surgery or necropsy might well destroy all evidence of an underlying tuberculous process. This point was well brought out by one case of proven tuberculosis that presented

with a pericardial effusion from which tuberculous organisms were grown; yet extensive resection of constricting pericardium some time later during surgery revealed no macroscopic or microscopic evidence of tuberculosis. Another example is a case who required two attempts at surgery to relieve him of cardiac constriction. The histology at the first operation revealed tuberculous granulation tissue, whereas the second showed fibrous and chronic inflammatory tissue only. Two of the 11 cases (one a Bantu youth of 19 were admitted for acute inflammatory 'idiopathic' pleural effusion with all the features usually associated with tuberculosis, and calcific constrictive pericarditis was incidentally found, for which surgery was performed.

There were 7 patients who presented with pericardial effusions which resolved, and in whom, with the absorption of the fluid, the signs of well-marked constrictive pericarditis developed. A long history of ill health, prolonged pyrexia, and response to antituberculous treatment, was present in all. One of these cases refused surgery, another died after operation, and both came to necropsy, where evidence of tuberculosis was not found, but an intense chronic inflammatory fibrous constriction of the heart was present.

A further 26 cases were assumed to be tuberculous because of the long history of chronic ill health, often dating from 3–12 months before admission. Over half of these had prolonged pyrexia, constitutional symptoms, and gradual resolution of all symptoms and signs while on antituberculous therapy. The pleural cavity was involved as well as the pericardium in the majority of cases and in 8 of them ascites (polyserositis) was also present, in the absence of cardiac constriction.

There were thus 44 cases who were regarded as probably tuberculous, though the aetiological diagnosis remains presumptive only.

The rarity of the condition amongst the Whites is again shown by its occurrence in only 3 cases (Table I). The majority of the cases (33) occurred in the Bantu; only 8 Coloured were affected. Most of the Bantu cases were encountered between the ages of 20 and 49 and there were 5 Bantu female cases.

3. *Pericarditis of Unknown Cause*

In 22 cases of pericarditis the aetiological diagnosis could not be determined and it was not possible with any degree of confidence to differentiate tuberculosis from 'virus' pericarditis. Examination of Table I shows that of these 21 cases 11 were Bantu, 6 Coloured and 5 White. Thus the overwhelming incidence of the disease in the Bantu is again manifest, particularly between the ages of 30 and 49. If anything, this suggests that tuberculosis is the commonest cause of pericarditis in this group, because virus disease, unlike tuberculous infection, is no respecter of wealth and privilege and indeed, is more often associated with the more favoured section of the population than the reverse. On clinical grounds, 9 cases were thought to fit better with the diagnosis of 'acute benign pericarditis'[8, 10, 13] in that the illness was acute in onset, sometimes associated with fever and upper respiratory symptoms, and of short duration. Recovery was rapid and complete, although 2 cases had many relapses over a period of several months before ultimately recovering. The pericarditis appeared to be 'dry' in 6 of these cases, since there was no increase in the heart size in association with the pericardial friction rub.

In 11 cases the clinical bias was towards tuberculosis but, in the absence of bacteriological proof or evidence of organ tuberculosis or severe systemic illness, no certain diagnosis could be made. The Mantoux skin reaction was of no help, because a positive reaction was obtained in most cases of pericarditis on whom the test was performed and, on the other hand, a negative Mantoux was occasionally encountered in a proven case of tuberculosis. The nature of the effusion was also not of any real help in diagnosis. Haemorrhagic effusions were encountered in 48 of 66 cases in which the nature of the effusion was noted, the quantity of blood varying from a slight staining to an amount that made the fluid appear to be venous blood, except that it did not clot and the packed cell volume was less than that of venous blood. A heavily blood-stained effusion was often associated with tuberculosis, but merely because tuberculosis was the usual cause of pericarditis. Haemorrhagic effusions, often fairly heavy, were encountered in pyogenic pericarditis, malignant pericarditis, and pericarditis of unknown origin; even in one case of myxoedema the pericardial fluid was haemorrhagic. There is often a traumatic element to the blood-staining of the pericardial fluid and, probably because of the constant action of the heart, the pericardial fluid soon becomes uniformly blood-stained.

The degree of diagnostic overlap between pericarditis of unknown or virus origin (including benign pericarditis) and tuberculous pericarditis is considerable, and certain diagnosis rests on bacteriological proof. Two cases are given below to illustrate the difficulty.

Case 1

J.M., a Bantu female of 42, was admitted on 2 June 1955 with a story that she had been quite well until 2½ weeks before admission, when she felt cold and shivery and sweated profusely, especially in the mornings on rising. Effort dyspnoea followed and progressed rapidly until she was orthopnoeic and suffered continuous pain in the chest and a feeling as if her chest had 'closed up'. Epigastric pain and pain in both flanks developed, more marked on the right, and she also complained of a backache felt in the lower thoracic region. A cough was present from the onset of the illness; at first it was associated with blood-stained sputum, but later it became extremely severe and she began to cough up large amounts of frothy white sputum with the features of pulmonary oedema. Anorexia was present from the onset of the illness and was associated with dysphagia, nausea and vomiting. Swelling of the legs and coldness of the feet completed the history.

On examination, she was seen to be obese and in great distress with orthopnoea. Marked oedema of the sacrum and legs was present with jugular venous distension but, because of the obesity, the venous pressure could not be measured. The liver reached 10 cm. below the costal cartilage and was tender. The peripheral pulses were small, with cold extremities, tachycardia, pulsus paradoxus and a blood pressure of 100/40 mm. Hg. The apex was impalpable, but dullness to percussion extended to the right and the left beyond the normal limits, with soft heart sounds and a distant triple rhythm. Bronchial breathing was present at both bases. There was no pyrexia and protein was present in the urine.

The ECG showed low voltage in the limb leads, with slight ST-segment depression and non-specific T-wave flattening over the left ventricle. The X-ray of the chest showed gross cardiac enlargement and bilateral pleural effusions.

Before aspiration could be performed she died suddenly in the early hours of the morning on the day of admission. At necropsy, extensive fibrinous pericarditis was found with at least 1,200 c.c. of deeply blood-stained haemorrhagic effusion in the pericardial cavity. Bilateral pleural effusions were present and the liver was congested. The visceral and subepicardial layers of the pericardium were thick and tough, and the myocardium and endocardium were macroscopically normal. The histological investigations showed organization of a fibrino-haemorrhagic pericardial effusion, with normal myocardium and no evidence of tuberculosis. Extensive

hepatic necrosis was present, and marked pulmonary oedema. The cause of the condition was not established, but tuberculosis appears to have been excluded, as no evidence of this disease could be found in the chest or elsewhere.

Case 2

K.M., a Bantu male between 60 and 70 years of age, was admitted on 2 July 1954. He had been quite well until 3 months before, when he began to notice effort dyspnoea, which progressed until, shortly before admission, he was considerably disabled. From the onset he had been having attacks of paroxysmal nocturnal dyspnoea. He had suffered with headache, vomiting and general ill-health for 2 months before admission. For the same period, he had been aware of abdominal discomfort and a stabbing pain in the left chest, pleuritic in nature, associated with a chronic non-productive cough.

On examination, he was found to be apyrexial. Pitting oedema of the sacrum and ankles was present, with moderate jugular venous distension and a 5-finger firm, tender hepatomegaly. The peripheral pulses were normal with a blood pressure of 180/70 and pulsus paradoxus. The apex could not be determined, nor were any cardiac pulsations present. Dullness on percussion was increased to the left and right and the heart sounds were normal. Fine basal crepitations were heard on both sides. Bilateral optic atrophy was incidentally found.

The ECG showed T-wave inversion in the anterior chest leads. On X-ray, bilateral basal effusions were seen, with enlargement of the cardiac shadow.

Five days after admission, 900 c.c. of blood-stained fluid was removed from the left pleural cavity, and 300 c.c. of fluid from the pericardial cavity, so heavily blood-stained that it was at first thought to be cavity blood. However, the fluid failed to clot and the haemocrit was lower than that of venous blood. After introduction of air into the pericardial cavity the effusion was clearly shown to be pericardial. Treatment was commenced with streptomycin, PAS and INH. After a month in hospital the patient's general condition had improved sufficiently for him to be transferred to a convalescent home, where he died suddenly the day after admission.

Necropsy showed a small amount of straw-coloured fluid in the peritoneum. The pericardium was markedly thickened, with complete obliteration of the anterior aspect of the sac by dense adhesions. The greater part of the sac contained laminated and organizing blood, with marked thickening of both layers of the pericardium. The outer surface of the heart was ragged, showing haemorrhagic areas, fibrous adhesions and organized blood clot. There was slight dilatation of the ventricles but, apart from this, the heart itself was normal. A marked splenomegaly and moderate hepatomegaly were present. The histology showed no evidence of tuberculosis in the pericardium or elsewhere.

Had these two patients not come to necropsy, the clinical diagnosis of tuberculous pericarditis would have been very reasonable. In both cases deeply haemorrhagic pericardial effusions were present and, in one case, there was a long history of preceding illness associated with left pleuritic pain. The cause of the pericarditis was not established but a bacteriological aetiology appears to have been excluded. A virus aetiology, e.g. Coxsackie,[14, 15] is possible but the condition could hardly be termed 'benign' pericarditis. The difficulty of making a definite diagnosis of tuberculosis in the absence of strong collateral evidence is emphasized. Price *et al.*[16] describe a case of death from cardiac tamponade with massive haemorrhagic pericardial effusion which they attributed to 'benign idiopathic pericarditis'. In a review of the literature they were able to find only 4 previously reported fatal cases.

4. *Pyogenic Pericarditis*

There were 17 cases of pyogenic pericarditis, purulent fluid being withdrawn in 4 on pericardial aspiration. The condition usually developed as part of a generalized septicaemic process. In 5 cases, it spread by contiguity from a lung abscess, pneumonia or empyema. Osteitis was the primary focus in 2, skin sepsis or abscesses with pyaemic spread in 5, and post-abortal sepsis in 3. In 1 case, infection followed a stab wound in the chest and in 1 no source of infection could be found, even after necropsy. The usual causal organism was *Micrococcus pyogenes aureus* (4), but others were streptococcus, pneumococcus and *Klebsiella pneumoniae*. In several cases the causal organism could not be identified.

All the patients were Coloured except for one White. No Bantu case was encountered in this series, though one case has subsequently been seen. Suppurative pericarditis appears thus to be rare in the Bantu, as is bacterial endocarditis. Most of the patients were under 30 and, though there were more males than females affected, there was less disproportion than in the other groups (Table I).

5. *Miscellaneous Causes*

The presenting symptom in 3 cases of malignant disease was pericardial involvement manifesting as acute chest pain. One patient required repeated aspiration to relieve him of tamponade, the primary lesion being in the lung; one developed pericarditis following on perforation of an oesophageal carcinoma; one was a young girl with intrathoracic lymphoma and extension to the pericardium.

A fourth case had well developed myxoedema. Routine screening of the chest revealed massive pericardial effusion which was producing no symptoms or signs of cardiac compression. The pericardial fluid was not inflammatory, although the protein content was 7 g.%. This patient recovered completely on thyroid therapy.

Comment

In the 160 cases of pericarditis, tuberculosis was far and away the commonest cause, with proof in approximately 50%. In another 25%, tuberculosis was the probable but not completely proven cause. In 13%, the cause of the condition was not known, though tuberculosis was favoured in many. Of the remainder, 10% were pyogenic in origin and 2% malignant.

OUTCOME

1. *Tuberculous Pericarditis*

Of the 73 cases of proven tuberculous pericarditis, 74% (54) were admitted with effusions, 18% (13) with established constriction, and 8% (6) with ECG evidence of pericardial involvement as part of the generalized tuberculous process. 45% (33) developed constrictive pericarditis and 50% (37) came to surgery (Fig. 3A). 16% (12) died.

Of the 54 pericardial effusions, 60% (33) developed constrictive pericarditis as the effusion resolved, of which the majority (28) came to surgery. Of the 5 cases who did not, 2 died of the effects of cardiac constriction and 3 passed through a phase of constriction which was as intense as most of the surgical cases, but after a long period of morbidity eventually recovered

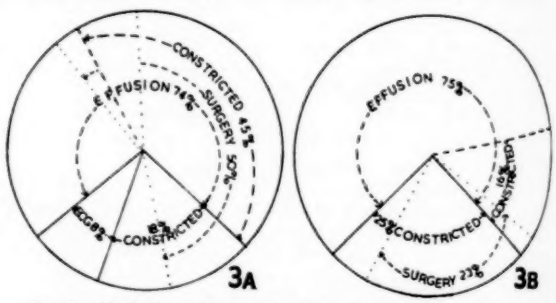

Fig. 3. (A) Tuberculous pericarditis, 73 cases (see text). (B) Probable tuberculous pericarditis, 44 cases (see text).

completely. The very high percentage of patients developing constriction in this group of cases may in part be explained by the fact that absolute proof of tuberculosis was frequently obtained at surgery and this led to inclusion of the case in this group. A very high incidence of constriction, however, was found in cases with a pericardial fluid positive for tuberculosis. Thus, of the 13 such cases, 9 came to surgery, 1 died and 3 recovered, though 2 of the latter went through a phase of constriction. 30% (15) of the patients with effusions completely recovered and returned to full health. Of the remaining 6 patients, 2 died during the early stages of the disease, 2 died of the effects of chronic cor pulmonale due to associated chronic pulmonary tuberculosis, and 2 came to surgery. One patient recovered completely from pericarditis with effusion, and surgery $2\frac{1}{2}$ years later for lung abscess revealed no pericardial pathology.

Of the 13 cases presenting with constriction, 7 came to surgery, 3 recovered without surgical intervention, 2 died, and 1 remained unchanged during the period of observation.

The 6 patients with ECG evidence of pericardial involvement as part of the generalized tuberculous process recovered completely on prolonged antituberculous treatment, with recovery of the ECG.

2. *Probable Tuberculous Pericarditis*

Of the 44 cases of probable tuberculous pericarditis, 75% (33) were admitted with effusions and 25% (11) with established constriction. 16% (7) developed constriction, 23% (10) came to surgery (Fig. 3B). 7% (3) died.

Of the 33 effusions, 21% (7) developed constrictive pericarditis as the effusion resolved, but only one of these came to surgery; 4 passed through a phase of constriction but after a long period of morbidity eventually recovered completely; 2 died of the effects of cardiac constriction; 70% (23) recovered completely and returned to full health. The remaining 3 cases were lost sight of before they had completely recovered, and could not be traced.

Of the 11 cases presenting with constriction, 9 came to surgery and 2 remained in chronic constriction for as long as they were observed. There were 4 cases with fairly marked pericardial calcification.

3. *Pericarditis of Unknown Cause*

Of the 22 cases in this group, 2 died and came to necropsy (details outlined above); the remainder recovered completely with no sequelae, apart from a persistently abnormal ECG in the occasional case. Effusions were present in 13, and 1 had an asymptomatic partially calcified pericardium, which remained unchanged.

4. *Pyogenic Pericarditis*

Of the 17 cases, 5 died of sepsis or cardiac tamponade. The remainder recovered completely, with 1 exception, who was left with mitral incompetence resulting from an associated acute bacterial endocarditis. An interesting finding in 2 cases was a persistently abnormal ECG as the only evidence of past cardiac involvement. No case of cardiac constriction was encountered in this group.

PROGNOSIS

Pericardial Effusion (*Tuberculous, Probable Tuberculous and Cause Unknown*)

The usual case of pericarditis, on admission to the wards, has a pericardial effusion, of which the aetiology is at first not clear. The majority are in fact tuberculous (see above) and in this series were treated as such. There were 100 cases presenting with pericardial effusion. Cardiac tamponade during the florid effusive phase was a common finding, but usually the effusion resolved or was aspirated and all evidence of interference with cardiovascular function disappeared. However, 40% developed constrictive pericarditis with the absorption of the effusion (Fig. 4A). This figure is unduly high because of special selection of the material. Groote Schuur Hospital is the centre for cardiac surgery of the whole Cape Province and cases who develop constrictive pericarditis during the course of their illness elsewhere are referred for surgery to this hospital. Thus, 8 of the 40 cases who developed constrictive pericarditis were referred for

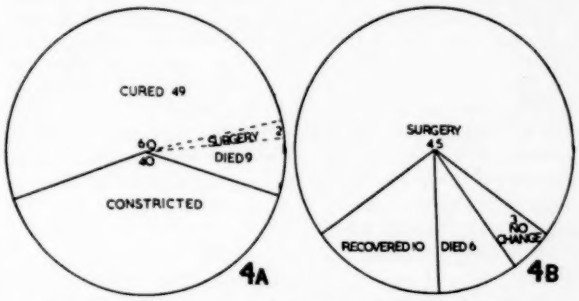

Fig. 4. (A) Prognosis in 100 cases of pericardial effusion (see text).
(B) Prognosis in 64 cases of constrictive pericarditis (see text).

special treatment. These cases in themselves probably represent only a small percentage of the total number of cases of effusion occurring in other centres. Of the 92 local cases admitted to this hospital with effusion, 32 developed constriction. All cases who recovered completely from the acute illness without the development of cardiac constriction remained well throughout the period of observation. It was possible to see 57 of the 60 patients for periods ranging from 1 to 6 years at repeated intervals and in these no form of cardiac involvement was observed to develop, once the patient had recovered from the acute stages of the disease. Of the 57 patients, 48 were enjoying full health and living an active life at their last examination, 7 having died during the acute phase of the disease and two many months later of chronic cor pulmonale, resultant on chronic fibroid pulmonary tuberculosis.

Constrictive Pericarditis

There were 64 cases of constrictive pericarditis, of whom 40 had been observed to go through the stage of effusion to constriction and 24 had presented with constriction. Of these, 45 came to surgery, 6 died of constriction, 10 spontaneously improved and completely recovered, and 3 were unchanged during the period of observation (Fig. 4B).

TREATMENT

Medical Treatment (*Tuberculous, Probable Tuberculous and Cause Unknown*)

(*a*) *Antituberculous therapy.* Antituberculous treatment was given in 80% of the cases and in 52% it was continued for a period of 6 months to 2 years or more. The treatment consisted in all cases of 1 g. of streptomycin daily, usually for

several months, 8–20 g. of PAS daily and INH in the usual dosage of 300 mg. daily. All three drugs were used together or in rotation in 77% of the treated cases. The development of constrictive pericarditis while on treatment did not seem to depend on what combination of drugs was used; it occurred with streptomycin and PAS, with streptomycin and INH, with streptomycin, INH and PAS, or even when no treatment at all had been given. Though it could not be proved, the impression was gained that constriction occurred more rapidly while patients were on antituberculous therapy and that before the introduction of the antituberculous therapy the development of constriction, if the patient survived the infection, appeared to have taken longer. Even when constriction occurred within 6 weeks, surgery revealed dense fibrous and granulation tissue. Though the simultaneous occurrence of pulmonary tuberculosis and tuberculous pericarditis was seen in 7 cases, tuberculous sequelae after the patient had recovered from pericarditis were uncommon and occurred only twice. Thus, one case developed Addison's disease and diffuse glandular and pulmonary tuberculosis 18 months after he had recovered from pericardial effusion which had not been treated. The other developed pulmonary tuberculosis while in a mental asylum 2½ years after recovering from constrictive pericarditis. Apart from these two exceptions patients remained free from tuberculous manifestations throughout the period of study.

(*b*) *Corticoid therapy*. An attempt was made to assess whether the administration of corticoids would prevent the development of cardiac constriction. While under antituberculous cover, cortisone was prescribed with a loading dose of 300 mg. and a maintenance dose of 100 mg. daily for several weeks. At a later date, 60 mg. of prednisone a day with a maintenance dose of 20 mg. was substituted. There were 14 cases of pericardial effusion selected for treatment with 14 alternate control cases receiving antituberculous treatment alone. No difference in outcome was noticed between the two groups. Of the 14 cases receiving corticoids and antituberculous treatment 4 developed severe constrictive pericarditis requiring surgical interference. The post-operative healing appeared to be somewhat delayed, but there was no spread of the tuberculous process in these cases. One patient who was mentally abnormal before treatment developed a psychosis during the post-operative period, but this gradually settled.

(*c*) *Cardiac therapy*. Treatment with digitalis was routine wherever evidence of tamponade or of cardiac constriction was present. In a few cases only it was administered alone with good resultant diuresis, but generally speaking mercurials were used at the same time. Though diuresis was usually obtained, the evidence of cardiac constriction remained unchanged in that the jugular venous pressure remained elevated and the liver remained distended. These drugs, however, helped to get rid of oedema and fluid in the serous cavities and temporarily relieved the urgent symptoms.

Surgical therapy

Of the 139 cases under discussion, 47 came to surgery and will be described in detail elsewhere.[17] Two of these patients were operated on during the phase of pericardial effusion. In one, the first of the series, the patient was collecting fluid rapidly after repeated effusions, the signs of cardiac tamponade remained unrelieved, and constitutional symptoms and pyrexia persisted, despite intensive therapy. At surgery, the parietal pericardium was removed and the fluid drained. The patient, however, failed to respond to treatment and ultimately succumbed with secondary infection and multiple bone sinuses. The second patient received antituberculous treatment for 6 months, during which period fluid accumulated rapidly, requiring repeated paracenteses, and he was bedridden. The parietal pericardium was markedly thickened and the signs of tamponade persisted. Surgery was eventually advised. The parietal pericardium was excised and the thickened fibrinous visceral pericardium partially removed. The post-operative course was gratifying, with immediate recovery, and long-term follow-up showed complete disappearance of all symptoms and signs. The remaining 45 cases can be subdivided into a group of 32 where constriction had been present for under 1 year, and a group of 12 where it had been present for more than 1 year.

In the first group, surgery was advised in patients who had passed through the fluid phase of pericardial effusion and had developed constrictive pericarditis. The period required to pass from the effusive to the constrictive phase varied from 6 weeks to several months. Almost all the patients were labourers whose livelihood required them to return to full activity as soon as possible. It is probable that after a prolonged illness resolution would have occurred in some of the surgical cases, as took place in several patients who refused surgery and ultimately recovered completely. With surgery, however, the period of morbidity is markedly reduced and the recovery rate high. Two patients required 2 surgical attempts each before they improved. Patients were regarded as cured if they were completely symptom-free, the jugular venous pressure was normal, and there was no hepatomegaly, no abnormal findings on clinical examination, and normal cardiac movement on radioscopy. Full return of the ECG or X-ray to normal was not included amongst the criteria of cure. 86% (26) were completely cured, with return to full heavy labour and no recurrence over a prolonged period of observation. If the patient was symptom-free but signs of cardiac constriction, viz. slight jugular venous distension and hepatomegaly, persisted, the result was regarded only as improved; this was the position in 2 cases. One patient developed constriction again, but refused re-operation. Three died, 1 of massive post-operative pulmonary embolism 10 days after surgery, 1 of exhaustion following an acute toxic psychosis, and 1 of uraemia, surgery having been advised as a desperate measure because of rapidly increasing renal failure.

In the second group, the patients had been constricted for over a year but only one case had probably been constricted for many years and had cirrhosis of the liver. Nine were regarded as cured and 3 as improved; 2 required re-operation before they were cured and calcification was present in 4.

The jugular venous pressure and hepatomegaly did not improve as a rule immediately after surgery though symptomatic improvement often preceded objective change. It often took from weeks to months before the venous pressure gradually returned to normal and the liver returned to its normal size. Antituberculous therapy was continued in all the tuberculous cases and in most of the unproven cases for many months.

Of the 47 cases submitted to surgery, 35 were completely cured, 7 improved, 4 died and 1 re-constricted; 4 patients required re-operation.

DEATHS

In the 139 cases of pericarditis (tuberculous, probable tuberculous and of unknown cause) there were 16 deaths (11%). Four died as the result of the underlying tuberculous disease, 4 of the effects of constrictive pericarditis, and 4 after surgery. There were 2 deaths from pericarditis of unknown cause. Two patients died after pericardial aspiration—1 after the removal of a large quantity of fluid, presumably from acute cardiac dilatation, and 1 a week after instillation of air into a cardiac chamber followed by cerebral air embolism. (Pericardial aspiration is not without risk and during the last 2 decades 3 deaths have occurred in this institution after the needling of cardiac failure of unknown cause to exclude pericardial effusion.) One patient died several years after a surgical cure from an unassociated condition.

SUMMARY AND CONCLUSIONS

1. A series of 160 consecutive cases of pericarditis occurring during a period of 5 years were studied and their course followed. The possible period of observation to date of writing varied from 1 to 6 years. The follow-up was considered adequate in 94% of the cases. Pericarditis due to rheumatic fever, collagenosis, uraemia and cardiac infarction were excluded.

2. The incidence of pericarditis was unquestionably highest in the Bantu. In the Coloured the disease is common, whereas in the White it is rare. When it is remembered that the White and Coloured in Cape Town are each 5 times as numerous as the Bantu the markedly disproportionate involvement of the latter becomes more evident. In all races and almost in every decade males far outnumber females, and this is not due solely to the disproportionate number of males in the Bantu population. The malady is commonest from adolescence to middle age.

3. The diagnosis was made in the majority of cases on the history of chest pain, the presence of a pericardial friction rub, aspiration of the effusion, surgery, or necropsy. Almost all cases presented either as pericardial effusion or as constrictive pericarditis, though the development of constriction in a case of effusion was common.

4. Tuberculosis was found to be the commonest proved cause of pericarditis, accounting for 50% of the cases. In another 25%, tuberculosis was the probable, but not completely proved, cause. In 13% the cause of the condition was not known, though tuberculosis was favoured in many. Of the remainder, 10% were pyogenic in origin and 2% malignant.

5. Of the cases of proved tuberculosis, 75% presented with effusion and 18% with constriction. There was a high incidence of constriction (60%) in the cases presenting with effusion, so that ultimately over 60% of this group of cases developed constriction. Cases with a pericardial fluid positive for tuberculosis are particularly liable to constrict and this occurred in 11 of the 12 patients that survived long enough for this to develop.

6. Of patients with probable tuberculous pericarditis, 75% were admitted with effusions and 25% with established constriction. The development of constriction in this group of cases with pericardial effusion was less common, occurring in 16% so that ultimately 40% of this group were constricted.

7. There were 22 cases of pericarditis of unknown cause with 20 complete recoveries. Two died; their clinical and necropsy findings are described. The aetiology was regarded as virus but the outcome belied the use of the term 'benign pericarditis'.

8. There were 100 cases of pericardial effusion of tuberculous, probable tuberculous and unknown cause. Constriction occurred in 40%. All patients who recovered from the acute illness without the development of constriction remained free of all cardiac signs or symptoms (apart from occasionally persistent ECG abnormalities) throughout the period of study.

9. There were 64 cases of constrictive pericarditis, 40 of whom had been observed to pass from the stage of effusion to constriction. Surgery was performed on the majority, but 10 cases improved and recovered completely on antituberculous treatment alone.

10. Prolonged antituberculous treatment was given in the majority of cases and appeared to promote the development of constriction. Corticoid therapy was ineffective in preventing this. Though active pulmonary and organ tuberculosis associated with pericardial effusion was not rare, the subsequent development of tuberculosis once the condition had settled was exceptional and occurred in only 2 cases.

11. Surgical treatment was highly successful in relieving cardiac constriction and reducing morbidity. The operative mortality was low and re-constriction rare.

12. Patients with pyogenic pericarditis either succumbed during the acute illness or recovered completely, though the ECG occasionally failed to return to normal.

I wish to thank the medical staff of Groote Schuur Hospital and Somerset Hospital for their cooperation, particularly in allowing me to study and follow up their cases, and Dr. J. Burger, the Superintendent of Groote Schuur Hospital, for permission to publish the findings. My special thanks are due to Mr. W. Phillips, who performed the surgery. I wish to thank Dr. Maurice Nellen and Dr. L. Vogelpoel for their assistance with the management of many of the cases, and Dr. L. Mirvish and Prof. J. F. Brock for their encouragement. Miss A. D. Moodie gave invaluable assistance in tracing reluctant patients. Support for this study was obtained in part from the South African Council for Scientific and Industrial Research and the City Council of Cape Town.

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THE EXCRETION OF DRUGS, PESTICIDES, AND RADIONUCLIDES IN MILK

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In a previous article in 1947, the author[55] dealt with the limited information available on the excretion of drugs in human milk; subsequent articles by others[42,33] have indicated the same state of affairs. In spite of the tremendous increase in the number and use of therapeutic agents in the last decade a study of the recent literature reveals that little work has been done on their excretion in milk. In the present article an account is given of the information that has become available since 1947. A previous statement[55] still holds, that there is no information at all on the excretion in milk of many substances used in therapeutics, and that details about others on which reports have been made are very inadequate. Although it is clear that the excretion of many drugs in the milk has not been examined it should also be noted that many drugs will not appear in the milk because they are rapidly bound to plasma protein, inactivated, or cleared.

Consideration is also given in the present article to the possible dangers from cow's milk. The widespread use of fresh and dried cow's milk which may nowadays contain antibiotics, insecticides and radio-active substances necessitates the fullest investigation and constant surveillance of all milk preparations.

Attention is drawn to the following useful articles on the composition of normal milk. A detailed account of 73 components of human colostrum and milk with many references to the literature is given by Macy.[40] Clinical and chemical studies on human milk during lactation are reported by Hytten[30,31] and Hytten and Thomson.[32] The influence of diet and special feeds on the composition of cow's milk is reviewed by Petersen.[52] The chemical composition of breast milk, and of cow's, goat's and sheep's milk is given in full detail in Documenta Geigy (*Scientific Tables*).[20]

Pharmacological Data

Fluids administered in large amounts to women (at least 6 pints a day) do not increase milk production and may actually reduce it.[34]

Food constituents. The milk may acquire the odour of alliaceous oils when these are present in the mother's food. Cow's milk may taste of onions or smell of garlic when the animals have eaten onion grass or wild garlic.[52] When animals are given large amounts of cod-liver oil the milk may taste and smell of fish oil. There is little evidence that any products from fruit and vegetables enter the milk and cause symptoms in the baby. However, protein substances may be responsible for allergic reactions in the sensitive child, for instance, from egg albumin. The milk of mothers suffering from beri-beri is stated to be 'toxic' to the child,[33] but protection would be afforded by giving proper food.

Antibodies are present in human colostrum and in mature milk but they apparently do not survive digestion in significant quantities. In the human species the transfer of antibodies across the placenta is much more important than their ingestion in colostrum and in mother's milk. The presence of Rh antibodies in human milk was first demonstrated by Witebsky *et al.*[65] They found that the titre is usually low and that breast feeding causes no continued haemolysis of the baby's red cells. The titres of various antibodies in milk have been correlated with those in the blood stream by Davidsohn.[19] All blood-group antibodies, including the Rh agglutinins, may be excreted in the milk, and it is possible that a newborn infant with haemolytic disease may be further injured by the mother's milk; Dahr and Wolf[18] state that infants with erythroblastosis should not be nursed by their mothers. The view has been held for decades that infants with erythroblastosis do not thrive on their mothers' milk but this theory does not appear to be accepted nowadays; antibodies present in the mother's milk are inactivated in the intestinal tract and do not cause further haemolysis of the infant's red blood corpuscles. Immunity to the Coxsackie group of viruses is transmitted from vaccinated mice to their offspring in the colostrum or milk.[46]

The Excretion of Drugs

Depressants of the nervous system were considered previously[55] and there is little to add today except for the following details. Other groups of drugs are dealt with more fully.

Chloral hydrate administered in suppositories to nursing mothers was found, together with its metabolites, within 15 minutes and for up to 24 hours in the milk in levels lower than that in the maternal blood and in insufficient amount to affect the infant adversely.[3]

Morphine is not excreted in the milk or, if excreted, in insignificant amounts. The characteristic odour of opium may be transmitted to the milk.[59]

Pethidine is not excreted in the milk of rats.[59]

Caffeine is secreted in the milk, and may cause restlessness in some infants.[62] The widespread consumption of caffeine in various hot and cold drinks warrants further investigation of this subject.

Nicotine was previously considered[55] and shown to be a rare cause of symptoms in the breast-fed infant. Further references on nicotine are given by Goodman and Gilman.[28]

Antihistamines or their breakdown products only pass into the milk in minimal amounts and produce a lactagogue effect within 1 hour after injection, which is maintained for 24 – 72 hours.[53]

Fluoride was found rather constantly in milk at about one-third of the level in the mother's blood.[29] The level was not influenced by the ingestion of fluorides by the mother; for example, when sodium fluoride was taken in doses of 10 mg. daily for 5 days the maternal level increased but the amount in the milk remained approximately the same.

Iron is present in human milk to the extent of about 2·5 mg. per litre and in cow's milk, on an average, 0·5 mg. per litre. The amount in cow's milk is not influenced by the administration of iron to the animal. In puerperal women the administration of iron leads to an increase in the daily elimination of iron in the milk, reaching a peak about the 7th day of the puerperium, and more marked in primiparae than in multiparae.[24] The iron supplies of the

newborn infant may possibly be increased in this way by giving iron to lactating women.

Folic acid increases lactation in nursing rats, and liver is still more efficient in this respect.[48]

Dicoumarol administered in large doses to lactating rats, has produced haemorrhages and death in the suckling rats.[25] In rabbits the excretion of dicoumarol in the milk depresses the prothrombin index of the litter to a level lower than that of the mother.[23] When full controlled therapeutic doses are given to women some of the anticoagulant is secreted in the milk, but without significantly altering prothrombin activity in the infant.[1,7] On the other hand, Christ[10] states that dicoumarin derivatives pass readily into woman's milk and may cause harmful effects, including liver damage, in the infant; he concludes that ethyl biscoumacetate (tromexan) and other dicoumarol derivatives should not be given to women who are breast-feeding their infants.

Vitamin A increases considerably in the milk of normal lactating women within 12 hours after administration in aqueous dispersion, but the increase is much smaller when the same vitamin is given in oily solution; the aqueous preparation also produces higher blood levels, indicating good absorption.[58] The occurrence of carotenoderma in mother and infant was previously reported.[61]

Vitamin D in milk can be increased to an antirachitic amount by giving large doses to the mother.

Tocopherol added to the feed of dairy cows increased the fat content and the yield of milk.[27] According to Neuweiler[49] cow's milk contains vitamin E in amounts of 18 – 152 micrograms per 100 ml. and human milk 280 – 3000 (average 1000). Overdosage with 240 mg. of vitamin E (ephynal) daily only raised the milk to a higher physiological level. The needs of a suckling baby were estimated to be about 5 mg. a day, and this must come mainly from the food; it should be noted that cow's milk contains only a small amount of the vitamin.

Ascorbic acid can be increased up to 6 times its previous concentration when the maternal diet is rich in the vitamin but, under the best conditions, 8 mg. per 100 ml. is the maximum amount in breast milk.[11] Human milk usually contains 2 – 6 mg. per 100 ml.

Pyridoxine in human milk can be increased considerably by oral administration of this vitamin.[50]

The vitamin content of human milk and its fluctuations according to diet and supplements were studied during the War by Kon and Mawson.[37]

Thyroxine or iodinated products given to cows stimulate milk production and increase the amount of fat, lactose, and phosphorus, but little if any thyroxine is present in the milk and it is safe and suitable for human consumption.[5] In pregnant rats the administration of large amounts of thyroxine does not cause its secretion in a physiologically active form.[29]

Antithyroid drugs, both thiouracil and imidazole compounds, are excreted in high concentration in milk. In women the milk may contain 3 times as much thiouracil as the blood.[33,64]

Iodide is normally present in milk in small amounts, and the quantity is increased after oral administration of iodine compounds.

Radio-active iodine has been demonstrated in the milk of lactating mothers after oral administration of tracer doses of the isotope. The amount in the milk may be considerably higher than that in the plasma, i.e. there is selective concentration in the milk.[47] The risk of adverse effect on the infant thyroid is considerable. Nurnberger and Lipscomb[51] demonstrated a significant uptake by the thyroid glands of suckling infants. They also refer to earlier experimental work in mice and rabbits and other animals in which not only radio-iodine but also other isotopes such as radiocalcium, radiostrontium, radio-iron, and radiosodium were shown to be transmitted in the milk. In goats it has been found that when sodium radio-iodide is administered orally an average of 50% of the dose is found as iodide in the milk, and none is present as thyroxine or other organic compounds.[66]

Copper is present in human milk in concentrations up to 0·28 mg. per litre. In cow's milk the average concentration is 0·15 mg. per litre and this is not increased by giving 5 times the normal amount in the food. In rats the milk contains 10 times as much copper as the milk of other species.[59]

Selenium has been demonstrated in the milk of cows in seleniferous areas. In white rats injected with sodium selenate (containing radio-active selenium) the selenium is found in the milk bound to the proteins.[43]

Thallium may be present in toxic amounts for sucklings in fatal cases of thallotoxicosis.[12]

Sulphonamides. The excretion of these chemotherapeutic drugs into human milk received much attention in previous years.[55]

Antibiotics administered to cows pass from ingested food into the blood stream and thence into the milk. Some workers[56] reported that no penicillin was found in the milk of cows given intravenous injections of the drug, but others[35] describe the levels of penicillin in the milk after intramammary injection during the lactation period. The following antibiotics could be demonstrated in cow's milk after treatment of the animal for mastitis, but in amounts unlikely to modify oral or intestinal flora or resistant strains or to provoke sensitization: penicillin, detectable for 6 days; streptomycin, for 1 day; oxytetracycline, for 3 days, and chlortetracycline, for 3 weeks.[63] Penicillin has been found in human milk in significant amounts within 1 hour after injection, thereafter increasing in concentration to 4 hours and then gradually falling.[54] Streptomycin is excreted in the milk. Chloramphenicol reaches levels in the milk of human beings of about one-half those in the blood.[57]

Many authorities consider that the presence of antibiotics in milk and milk products may sensitize certain individuals and even perhaps cause reactions. This problem is important, especially in connection with penicillin, and steps have been taken to avoid this hazard.[21, 44]

Organic arsenicals given by parenteral injection are excreted in small amounts in the milk, and *mepacrine* in negligible amounts.[26]

Pesticides

Phosphate-ester insecticides are among the most toxic chemicals commonly used for pest control. They are not used on livestock.[13] One of these anticholinesterases named parathion was administered in capsules to dairy cows but did not pass into the milk and produced no harmful effects in the animals.[17]

Dicophane (DDT) is a chlorinated insecticide which is excreted in measurable amount in the milk of dairy animals which eat fodder from fields dusted with this compound. The milk may be lethal to insects and may produce typical symptoms in the sucklings of white rats and goats.[60] The milk of cows fed on sprayed alfalfa contained about 3·5 mg. per litre, which diminished in 10 days but persisted for 4 – 6 months after withdrawal.[4]

Gamma benzene hexachloride (lindane) is eliminated in the milk of lactating animals, most of it within 24 hours after administration is stopped. It is rapidly excreted and completely disappears from the animal's body within one or two weeks.[14]

Toxaphene is a chlorinated camphene used to destroy ticks and mites. It may be excreted in the milk.[15] It should not be used on dairy cattle or in barns.

Chlordane, fed to lactating rats, causes the milk to be toxic to the suckling. There is danger associated with its ingestion and retention in milk, or in the body tissue of dairy animals, poultry, or meat animals.[16] *Dieldrin*, another indane derivative, passed into the milk when sprayed on cows at 3-week intervals but the amount gradually decreased, regardless of its continued application.[8]

Phenothiazine has been used as an insecticide and as an anthelmintic in livestock. It caused the milk of nursing goats to undergo pinkish discolouration when exposed to the air for several hours.[22]

Radio-active Substances

Reference has been made above to radio-active iodine and other isotopes.

Radio-active materials (radionuclides) created as the result of nuclear detonations (atomic bombs) have been carried to the stratosphere and return slowly to earth with rain, snow and dust particles. One danger is their passage through the soil into plants. In cows the milk can become radio-active from this source. There is constant need for radiation surveillance of milk, dairy products, and other foods. Any determined values and variations must be considered tentative and subject to change when estimates are made of the possible hazards associated with the long-term use of radio-active milk.

The fall-out of radio-active strontium, its presence on grass, its absorption into animals, and the concentration in milk, and in the bones of sheep, have been measured in England.[45] The amounts estimated in hay and milk have this year been published by Booker.[6] About 1/7th of the strontium-90 ingested by the cow appears in her milk. Experimentally it has been demonstrated in lactating rabbits that radio-active strontium passes through the milk to the suckling; the peak of excretion in the milk occurs when the level in the blood is low.[36] In lactating guinea pigs the intramuscular injection of radiostrontium causes its appearance in the long bones of the sucklings.[41]

The presence of caesium-137 and the variation in amount of this radionuclide in dried milks in England is revealed by Booker.[6] It appears to be derived mostly from direct fall-out on the herbage and little from the soil.

In the USA dried milk is sampled from numerous places for caesium-137 and potassium-40 as a routine measure. Traces of these isotopes have been detected in human beings, the main source probably being cow's milk.[2]

In Sweden the presence of caesium-137 in dried milk and soil has been determined[39] and the correlation between caesium-137 and strontium-90 shown to be good, so that the caesium-137 values may be used for estimations of the strontium-90 content, provided their source is atomic-bomb debris.

During periods of local weapon-testing, barium-140 appears prominently in milk.[2] Data have been published this year on the concentrations of radio-active iodine, strontium, barium and caesium in cow's milk in the USA.[9,38] The radionuclide of greatest potential hazard in milk is ^{90}Sr, followed by ^{131}I. In addition, further evidence is needed on the contribution of radionuclides in other foods towards total dietary exposure.

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A SURVEY OF PENICILLIN CONTAMINATION OF MARKET MILK SUPPLIES

P. J. MEARA, D.V.Sc., *Johannesburg*

Although attention was previously directed to the subject of antibiotic contamination of the milk supply as a veterinary and public health problem[1,2] information is still lacking in regard to South African milk supplies. An antibiotic survey of milk supplies has therefore been carried out as an initial step towards deciding whether the problem is worthy of further attention. The survey has been undertaken in respect of herd milk supplies received in Johannesburg from the Transvaal highveld area, with particular reference to penicillin contamination of the milk. The area of milk supply extends in a vast semi-circle stretching from Ermelo - Volksrust in the east, of Potchefstroom - Klerksdorp in the west, and as far south as Frankfort - Koppies in the Orange Free State.

The reason for concentrating on penicillin to the exclusion of other antibiotic preparations is threefold:

1. Penicillin is still extensively used for the intramammary treatment of bovine mastitis, in spite of the fact that other antibiotic preparations such as dihydrostreptomycin, aureomycin, terramycin, etc., are tending to supplant penicillin.

2. Many medical authorities in the field of antibiotic therapy, allergy and paediatrics believe that, of the various forms of antibiotic therapy employed for bovine mastitis, it is penicillin that is most likely to make the milk harmful to consumers.[3]

3. The presence of penicillin in milk is established relatively easily by an identification test using the enzyme penicillinase, which specifically inactivates penicillin.

Material and Method

Herd milk samples collected at random from Johannesburg dairies during the period November 1958 to June 1959 were subjected to a disc assay procedure based on the $\frac{1}{2}''$ double disc method of Cerny and Morris.[4] The test organism employed was a strain of *Sarcina lutea* obtained from the Department of Biological Standards, National Institute for Medical Research, London. The organism is sensitive to a low concentration of penicillin, of at least 0·01 units of penicillin per ml. of milk, by the procedure employed for this $\frac{1}{2}''$ double disc assay method.

The possibility that natural inhibitors in milk from untreated cows might produce false reactions (by bacteriophage and naturally occurring heat-labile inhibitory substances) was eliminated by preliminary heating of the milk to a temperature of 180°F for 5 minutes. When the milk is heated to this extent antibiotics which are present may be partially inactivated, and recent workers are content to employ a temperature of 180°F for only 1 minute.[5] The results obtained after heating the milk in this way do emphasize the fact, not generally appreciated, that the process of pasteurization normally carried out at 161°F for 10 seconds does not destroy antibiotic substances in the milk.

Whenever a zone of inhibition was noted the test was repeated for confirmation of the result, and an additional duplicate milk specimen treated with penicillinase was simultaneously tested in identical manner. The absence of inhibition in the penicillinase-treated sample was accepted as positive indication that the inhibitory effect of the normal sample was due to penicillin contamination.

Although the magnitude of the zone of inhibition was always recorded these comparative measurements are not employed here as a criterion of the concentration of penicillin in the milk, largely on account of the many variations in the *in vitro* tests that are difficult to control on a day-to-day basis.[6]

Results of Survey

The results are summarized in Table I. Of the 1,229 milk samples that were tested for penicillin contamination, 66 showed inhibitory characteristics (5·37% of samples tested). The cause of the inhibition was undecided in respect of 2·28% of the samples, and in the remaining 3·09% the inhibition was due to penicillin.

TABLE I. PENICILLIN CONTAMINATION OF HERD MILK SUPPLIES

No. of herd milk samples	1,229
No. of inhibitory milk samples	66 (5·37%)
No. of samples containing penicillin	38 (3·09%)

It was not possible to complete the penicillin identification procedure in respect of certain inhibitory milk samples. Especially during the December - February midsummer period a number of samples soured to such a degree as to invalidate the test by the time the penicillinase test was applied the following day. In yet other instances the inhibitory effect could not be reproduced, presumably owing to a dissipation of the inhibitory substances as a result of natural changes in the milk, perhaps assisted also by the preliminary heating process. There is however no doubt that a minimal proportion of at least 3·09% of milk samples considered typical of Transvaal market milk supplies were contaminated with traces of penicillin.

Comment

This limited survey shows that, as in Europe, the USA and Great Britain, penicillin traces are commonly present in a small proportion of South African herd milk supplies. It could hardly be otherwise in a country where the farmers can freely obtain antibiotic remedies for treating udder infections from chemists, agricultural cooperatives, veterinary firms and other agencies.

After intramammary therapy the antibiotic substance is not completely absorbed in the cow's udder and a quantity becomes excreted in the milk, commencing from the first milking after treatment. The amount of antibiotic is usually greatest at the first milking and then decreases progressively,

TABLE II. EXCRETION OF PENICILLIN IN MILK UP TO 3 DAYS AFTER INTRAMAMMARY THERAPY

Penicillin Dosage (units per quarter)	*Number of Samples*	*Units of Penicillin per ml. of Milk, after:*		
		24 hours	*48 hours*	*72 hours*
25,000	4	5·7	0·2	—
50,000	22	9·0	0·9	0·2
100,000	6	8·1	1·3	0·5

but effective quantities may remain for 3-5 days according to the preparation used and the dosage administered. The excretion of penicillin in milk up to 3 days after treatment with various rates of dosage is exemplified by the results obtained by Danish workers, as shown in Table II (Voordeckers[7]).

Dosage of 300,000 units is commonplace and a dosage of less than 100,000 units per quarter is seldom employed. These results afford some indication of the quantity of penicillin which may be present in the milk obtained from an infected cow shortly after treatment. For instance, after 24 hours a two-gallon cow treated in each of the 4 quarters with 100,000 units excretes about 74,000 units of penicillin, or approximately 2,000 units of penicillin in a glassful of milk.

The degree of contamination of the bulked herd milk supply ultimately depends on a number of factors such as the dosage administered, the number of quarters infused, the amount of milk produced by the infected cows, the number of infected animals in a herd, and the volume of milk from treated cows in relation to the total herd milk supply. In general terms, however, the interaction of all these variable factors, as well as the possibility of allergic or sensitizing ill-effects to persons consuming the milk, can be easily eliminated if the milk from each treated quarter is discarded or used for purposes other than human consumption for a period of 72 hours after treatment.

Control

The fundamental requirement is that the milk from an infected cow shall be withheld from the herd milk supply for 3 days after antibiotic treatment. Since the milk often *appears* to be normal shortly after treatment the farmer may believe that the milk is suitable for use, but apart from its antibiotic content such milk is also adulterated by pus and is generally unsuitable for consumption.[8]

Obviously there is need for considerable educational and propaganda work to overcome ignorance of this type. Another possibility, which may be of eventual assistance in ensuring the discarding of milk, is the incorporation of a suitable dye-stuff in the antibiotic preparation, in order to discolour the milk for a considerable period after treatment. Workers in the USA and Scandinavia have already achieved a limited degree of success in this direction.

Unfortunately there is at the moment no rapid platform test which can be used on the incoming milk to detect antibiotic contamination of milk supplies and to prevent their being used for consumption. Thus the control procedure would seem to depend essentially on the routine antibiotic testing of herd milk supplies, and subsequently either (*a*) possibly prosecution for supplying contaminated milk, or (*b*) suspension of the milk supply until the milk has been demonstrated to be free from contamination. As procedure (*b*) is likely to require several days to complete, the penalty is sufficiently severe to deter the dairy farmer from taking the risk of including doubtful milk in his herd milk supply.

SUMMARY

Samples of market milk supplies collected from dairies in Johannesburg were examined for penicillin contamination.

Penicillin in concentrations exceeding 0·01 units per ml. of milk was found in 3·09% of the 1,229 samples tested.

Acknowledgement is due to the City Dairy Inspectors of the Public Health Department for their cooperation in collecting milk samples, and to the Director of the Abattoir and Livestock Market Department, Johannesburg, for permission to make this publication.

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URINE AND STOOL INVESTIGATIONS IN THE DIFFERENTIATION OF THE PORPHYRIAS AS SEEN IN THE THREE RACIAL GROUPS IN CAPE TOWN*

L. EALES, M.D., M.R.C.P.

In the delineation of disorders of porphyrin metabolism the determination of faecal porphyrin is just as important as the estimation of urinary porphyrin. For a complete appreciation urinary δ-aminolaevulic acid (ALA) and porphobilinogen (PBG), determinations may also be required.

The investigation reported here includes estimations of urinary and faecal porphyrin in a series of normal subjects, in a group of patients with various disease states and, finally, in various porphyric disorders as seen in the 3 main racial groups—the White, the Cape Coloured and the Bantu.

1. *Normal Subjects*

A series of 70 apparently normal subjects of the 3 main racial groups in Cape Town was investigated. Twenty-four-hour urine collections and faecal samples obtained during or just after the collection period were analysed. Urinary uroporphyrin and coproporphyrin, and faecal coproporphyrin and protoporphyrin were determined in all subjects while ALA and PBG were determined in several of them.

Urine. In the White subjects average coproporphyrin and uroporphyrin concentrations were 42·5 and 7·4 μg./l. respectively; in the Cape Coloured, 33·1 and 6·5 μg./l.; and in the Bantu, 35·1 and 5·4 μg./l. The uroporphyrin fraction did not usually exceed 20 μg./l.

Faeces. Faecal determinations were expressed per g. dry weight of faeces. In White subjects the total faecal porphyrin averaged 41·0, the coproporphyrin 8·8 and the protoporphyrin 30·2 μg./g. dried weight. In the Cape Coloured the figures were 23·9, 6·3 and 20·1, and in the Bantu 44·9, 14·6 and 34·4.

It is believed that the often quoted upper limit of normal total porphyrin (50 μg./g. dried weight) is too low. The range for total porphyrin in all subjects studied is 0·2 – 137·6. The majority of determinations fall below 50 μg./g., yet there are several values above 100 μg./g. Protoporphyrin accounts largely for the total porphyrin. In Bantu subjects in the metabolism ward on the 'basic Bantu diet' stool porphyrins are very low, yet the addition of meat in one instance failed to increase faecal porphyrin.

2. *Subjects with Various Disease States*

Twenty-six cases with cardiac, renal hepatic, gastro-intestinal or endocrine disorders were studied. In 3 cases of cirrhosis of the liver there was a low faecal porphyrin concentration, but the urinary coproporphyrin level was markedly increased; other cases of hepatic disease had normal levels as a rule, but an abnormal amount of urinary uroporphyrin was found in 1 case each of primary and secondary carcinoma of the liver.

The results in cases of cardiac, renal, and gastro-intestinal disease were usually within normal limits, but high values for urinary uroporphyrin were encountered in a case of congestive heart failure due to aortic stenosis, and in another patient with cor pulmonale. In both patients the faecal porphyrin concentration was within normal limits.

3. *Cases of Porphyria*

The clinical presentation in 122 cases was reported (67 White, 35 Coloured and 20 Bantu). All had uroporphyrinuria. The

* Abstract of paper presented at Research Forum, University of Cape Town, 4 August 1959.

clinical presentation was denoted as acute, cutaneous, and mixed. (Mixed referred to cases with both cutaneous and acute symptoms.) In the White race the 3 clinical forms were encountered with more or less equal frequency, while almost all of the Bantu cases were examples of the cutaneous form. The Cape Coloured patients studied fell between these two extremes; cutaneous porphyria predominated, but acute and mixed forms were encountered.

Urinary and faecal porphyrin determinations were carried out in 30 White, 16 Cape Coloured, and 10 Bantu porphyrics. In addition urinary ALA and PBG were determined in many of these patients.

White porphyrics. Of 30 closely studied porphyrics 25 had markedly raised stool porphyrin concentrations (211 – 2303 μg./g.). These were all South African-born porphyrics and in the majority there was a positive family history. The remaining 5 patients had stool concentrations of 136 μg./g. or less and in each case there was a possible cause for this. Two had cirrhosis of the liver; 2 were not South African born—a Russian and a Norwegian—and the 5th was a case of cutaneous porphyria in a child.

Coloured porphyrics. Of 16 cases 9 had normal stool porphyrins and the remaining 7 had markedly increased stool porphyrins (181 – 8135 μg./g. dried weight), and in some of these cases a positive family history was obtained.

Bantu porphyrics. Of 10 Bantu cases 8 had normal faecal porphyrin concentrations (19·9 – 93·5 μg./g.). All except 1 had gross uroporphyrinuria. Urinary coproporphyrin concentration was also markedly increased but to a lesser degree. In 1 Bantu patient with acute porphyria the stool porphyrin concentration was very greatly increased.

Thus the Bantu patients had mainly increased porphyrin in the urine (and not in the faeces), and cutaneous forms of the disease predominated; in the White South African patients faecal porphyrin concentration was usually markedly increased, all forms of the disease occurred, and affected families were common. The Cape Coloured patients seemed to fall between these two groups both as regards excessive excretion or porphyrin in the stool and as regards clinical presentation.

The Swedish form of the disease which is rarely seen here has increased amounts of ALA and PBG in the urine most of the time. In South African genetic porphyria these substances occur in the urine in excessive amounts only during the acute attacks, viz., in a fatal case of fulminating porphyria the urinary ALA excretion reached 316 mg. per 24 hours. In the few Bantu subjects with cutaneous porphyria so far investigated no significant increase has been encountered.

Other means of differentiation (ALA loading and electrophoresis of urine porphyrins) are under investigation.

Further experience with a faecal screening test was also reported (red fluorescence induced by exposure to U.V. light of an acetic acid, ether, and amyl alcohol extract of faeces. The test was graded as follows: O yellow blue-green; ± doubtful tinge of red; + definite red fluorescence; and ++ brilliant red fluorescence). 610 stools from 582 patients with miscellaneous disorders were examined: O 416; ± 99; + 76; ++ 19. Of the 76 with a positive reaction 2 had genetic porphyria; this was also the case in no less than 14 out of 19 patients whose stools had brilliant fluorescence. If anything the test was too sensitive. The results of the test correlated fairly well with the faecal porphyrin concentration (U.V. spectrophotometric method).

The help of Drs. S. J. Saunders and E. B. Dowdle; the support of the South African Council for Scientific and Industrial Research and the Staff Research Fund of the University of Cape Town is gratefully acknowledged.

DERDE AKADEMIESE PERSONEELDAG VAN DIE KARL BREMER-HOSPITAAL EN DIE GENEESKUNDIGE FAKULTEIT VAN DIE UNIVERSITEIT VAN STELLENBOSCH

Die jaarlikse akademiese personeeldag sal op Donderdag en Vrydag 8 en 9 Oktober gehou word by die Geneeskundige Skool, Karl Bremer-Hospitaal, Bellville, Kaap. Die volgende is 'n voorlopige program:

REFERATE

Donderdag 8 Oktober

2.00 nm. Opening: Prof. F. D. du T. van Zijl en dr. R. L. M. Kotzé.
2.15 nm. Die uitwerking van monasiet op die longe van rotte: Mnr. B. F. Thiart en dr. J. L. Meiring.
2.35 nm. Longaanpasbaardheid: Dr. S. V. Potgieter.
2.55 nm. Jongste vordering by die behandeling van skimmelsiektes: Dr. J. Marshall.
3.15 nm. Teepouse.
3.45 nm. Bespreking van gevalle van porfirie in die Karl Bremer-Hospitaal: Dr. J. Stockenström.
4.05 nm. Etiologie en mikrobiologie van aktinomikose: Dr. H. Brede.
4.20 nm. Esofageale peristaltiek by die konyn: Dr. G. S. M. Botha.
4.40 nm. Die atoom- en waterstofbom soos gesien deur 'n medikus: Dr. J. P. de Villiers.

Vrydag 9 Oktober

8.30 vm. Die verspreiding van bloedgroepe by pasiënte van die Karl Bremer-Hospitaal: Dr. H. Brede.
8.45 vm. Kaliumverlies en spierverslappers: Dr. P. A. Foster.
9.05 vm. Die invloed van kolloïdale silika op die O_2-verbruik van weefsels: Dr. F. M. Engelbrecht.
9.25 vm. Filmvertoning.
9.55 vm. Vaskulêre fistels: Prof. A. J. Brink.
10.15 vm. Teepouse.
10.45 vm. Postpartum bloeding: Prof. J. N. de Villiers.
11.05 vm. Bespreking van L.E.-gevalle in die Karl Bremer-Hospitaal: Dr. C. L. Wicht.
11.25 vm. Aspekte van die behandeling van skoliose: Dr. J. Anderson.
11.45 vm. Panhipopituitarisme: Dr. P. W. A. Botha.
12.05 nm. Chirurgiese bespreking: Dr. J. J. W. van Zyl.
12.25 nm. Middagete.
2.00 nm. Kunsmatige hartkleppe: Dr. B. J. v. R. Dreyer.
2.30 nm. Voltydse ekstra-uterine swangerskap: Dr. J. P. du Toit.
2.50 nm. Filmvertoning.
3.30 nm. Teepouse.
4.00 nm. Hemo-dinamiese en miokardiale metaboliese uitwerking van die infusie van hipertensin-2-Peptiden by honde: Dr. L. Potgieter.
4.20 nm. Epidurale analgesie: Drs. R. D. Allan en P. A. Foster.
4.45 nm. Amniotiese longembolisme: Drs. J. J. de Wet en J. G. Steytler.
5.00 nm. Verkiesing van nuwe komitee.

Daar sal wetenskaplike sowel as farmaseutiese uitstallings wees.

IN MEMORIAM

LT.-COL. CHARLES PERCIVAL BLIGH-WALL, O.B.E., M.D. (Edin.)

Dr. Hamilton W. Dyke, C.B.E., of East London, writes: Dr. C. P. Bligh-Wall died in East London on 11 August 1959 at the age of 87 years.

Dr. Bligh-Wall was born at Paddington, Middlesex, England, on 7 October 1871 and received his early education at Bradfield College. His professional training was at Edinburgh University, where he graduated M.B., Ch.B. in 1897 and in 1905 obtained the M.D. degree of that University. Between 1897 and 1899, when Dr. Bligh-Wall came to South Africa, he held resident appointments at the Inverness Infirmary and Fever Hospital.

Dr. Bligh-Wall served with the British forces during the Boer War as a medical officer and was mentioned in dispatches by Lord Roberts.

After the War Dr. Bligh-Wall set up practice in Butterworth, Cape, and was District Surgeon there from 1904 to 1915. While

in Butterworth he was Superintendent of the local hospital and Mayor of the town.

As pioneer in radiological medicine Dr. Bligh-Wall received severe X-ray burns to both arms which led to the amputation of his left arm.

At the outbreak of the First World War Dr. Bligh-Wall became a medical officer with the rank of captain in the A.C.F. In August 1916 he was commissioned in the South African Medical Corps as a Captain and in April 1918 he was promoted to Lieutenant-Colonel A.D.M.S., GHQ, East Africa. He was twice mentioned in dispatches and was awarded the military O.B.E. in 1918 and was decorated in East London by Prince Arthur of Connaught in 1921.

After the War he was in practice in Kingwilliamstown where he was associated with the Grey Hospital. He retired in 1944 and settled in East London.

Throughout his professional career Dr. Bligh-Wall was an active member of the Medical Association. From 1927 he represented Kingwilliamstown on the Border Branch Council and from 1931 to 1944 he represented the Border Branch on Federal Council. In 1933 he was President of the Border Branch.

Dr. Bligh-Wall was a 'gentleman to the backbone', possessor of an old-world courtly manner, charm, and courage—this outstanding characteristic showed itself particularly in his later years, when in addition to the old-standing loss of his left arm, greatly impaired eyesight depriving him of vision and deafness preventing him from hearing radio programmes, he also underwent three major operations all of which he endured with amazing cheerfulness and lack of self pity.

Dr. Bligh-Wall is survived by his widow and two married daughters. He was buried at Kingwilliamstown on 15 August and the funeral service included Military Honours provided by the local branches of the B.C.E.S.L.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

PREDSOL PREPARATIONS

Glaxo Laboratories (S.A.) (Pty.) Ltd., in introducing certain new Predsol preparations, supply the following information:

Predsol Nasal Drops

Predsol nasal drops contain 0·1% prednisolone disodium phosphate in isotonic buffered solution. They are soluble and produce maximum therapeutic effect through contact with the inflamed tissues.

The nasal drops are indicated in the treatment of hay fever, vasomotor and non-seasonal allergic rhinitis. They are free from side-effects, but are contra-indicated in septic conditions of the nose demanding specific chemotherapy and if primary rhinitis has become secondarily infected. Predsol nasal drops are supplied in 10 c.c. bottles with droppers.

Predsol-N Nasal Spray

Predsol-N nasal spray contains 0·025% prednisolone disodium phosphate, 0·5% neomycin sulphate, and 0·025% naphazoline nitrate in an aqueous solution. It is indicated for use in various commonly occurring inflammatory allergic conditions of the nose.

Predsol-N nasal spray is supplied in 15 c.c. plastic spray bottles.

Predsol Skin Ointment No. 1, Predsol-N Skin Ointment No. 1 and Predsol Skin Lotion

Predsol skin ointment is non-greasy and contains 0·5% prednisolone disodium phosphate in a water-miscible base. Predsol-N skin ointment is also non-greasy and contains 0·5% prednisolone disodium phosphate with 0·5% neomycin sulphate in a water-miscible base. Predsol skin lotion contains prednisolone disodium phosphate in a transparent aqueous liquid.

These preparations are colourless, non-irritating and do not stain the skin. They are indicated in anal and vulvar pruritus contact dermatitis of various types, allergic eczema, food eczema, infantile eczema, eczematoid reactions of the eyes and ears, neurodermatitis, nummular dermatitis, and seborrhoeic dermatitis.

The ointments are supplied in 5 g. tubes and the skin lotion in a 20 c.c. plastic 'squeeze' bottle.

Predsol Drops and Predsol-N Drops for Eye or Ear, and Predsol Eye Ointment and Predsol-N Eye Ointment

Predsol drops for eye or ear contain 0·5% prednisolone disodium phosphate in sterile isotonic buffered solution. Predsol-N drops for eye or ear contain 0·5% prednisolone disodium phosphate with 0·5% neomycin sulphate in sterile isotonic buffered solution. Predsol eye ointment contains prednisolone disodium phosphate in a bland paraffin base. Predsol-N eye ointment contains 0·5% prednisolone disodium phosphate with 0·5% neomycin sulphate in a bland paraffin base.

These eye ointments are indicated for use in inflammation caused by trauma or other irritants. The ear preparations are indicated for use in inflammatory conditions such as otitis externa due to infection or other causes. In both eye and ear conditions Predsol-N preparations should be used when infection is present or suspected.

The drops are supplied in 3 c.c. vials with droppers and the eye ointment in 3 g. tubes with ophthalmic nozzles.

PASSING EVENTS : IN DIE VERBYGAAN

South African Society of Obstetricians and Gynaecologists, Cape Town Sub-group. At the Annual General Meeting of this Subgroup held on 3 August the following office bearers were elected: Chairman, Dr. D. P. de Villiers; Hon. Secretary, Dr. Fred Benjamin; Committee members, Drs. T. St. V. W. Buss, L. J. Abramowitz and P. F. M. du Toit.

* * *

Dr. H. S. Gear, who recently relinquished the position of Assistant Director-General of the World Health Organization, and is at present a member of the Rhodesia and Nyasaland Commission of Enquiry into the Health and Medical Services of the Federation, as well as Consultant to the Minister of Health on Federal Health Services, will succeed Dr. A. J. Orenstein in January 1960 as Director of the Pneumoconiosis Research Unit, South African Council for Scientific and Industrial Research. Dr. Gear was Deputy Chief Health Officer of the Union Health Department until 1951 and remains seconded from that Department. He is a Witwatersrand graduate, and served as medical officer in the Northern Rhodesia service and at the Lister Institute of Medical Research, Shanghai, before joining the Union Health Department. Dr. Gear will shortly resume a medical research survey on which he has been engaged in America and will be visiting the UK, Belgium, France and Germany.

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Cape Western Branch (M.A.S.A.). A special Branch meeting will be held on Thursday 8 October at 8.15 p.m. in the Physiology Lecture Theatre, Medical School, Observatory, Cape (telephone 5-2455). At this meeting Dr. Harold Stewart, Chief Pathologist to the National Institutes of Health, Bethesda, Maryland, USA, will speak on 'Some observations on the geographic pathology of cancer of the stomach in man'.

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Southern African Cardiac Society. Sir Russell Brock, of Guy's Hospital and Brompton Hospitals, London, will address a meeting on Friday 9 October at 8.15 p.m. in the Physiology Lecture Theatre, Medical School, Observatory, Cape, when his subject will be 'Cardiac surgery'.